Encyclopedia of Drugs, Alcohol & Addictive Behavior

Third Edition

HENRY R. KRANZLER & PAMELA KORSMEYER

ENCYCLOPEDIA OF

DRUGS, ALCOHOL & ADDICTIVE BEHAVIOR

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DRUGS, ALCOHOL & ADDICTIVE BEHAVIOR

THIRD EDITION

Volume 1

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PREFACE

The first edition of the *Encyclopedia of Drugs and Alcohol* (as it was first titled), published in 1995, was the product of a massive effort on the part of Jerome H. Jaffe and a group of distinguished colleagues that he, through his long experience and many friends in the various fields of addiction studies, was able to bring together. The result of the collaboration among the members of this original group was a compendium of information from every viewpoint and specialty having to do with the use and abuse of psychoactive substances. We, the editors of this third edition of the *Encyclopedia*, have attempted to remain true to Dr. Jaffe's original purpose as described in the preface to the first edition.

> The Macmillan *Encyclopedia of Drugs and Alcohol* has been written as a comprehensive source of information for non-specialists who have an interest in any of the diverse topics that are included under the broad general heading of substance use and abuse. While many of the entries are devoted to the actions of drugs on the body, the work as a whole is intended to serve the wider interests of social science and includes articles on social policy, history, politics, economics, international trafficking, law enforcement, scientific and medical research, treatment and prevention of drug abuse, and epidemiology.

The title of the second edition, published in 2001, was modified to include addictive behaviors that did not involve drugs or alcohol. While paying close attention to the original vision and the broader scope reflected in the title change, we have tried to update and expand the work to include new and emerging topics and important developments in the many fields of addiction studies. We have included information on recent scientific discoveries and theories in behavioral neuroscience, which help to illuminate how addictive substances and behaviors affect the brain and the impact of these effects on behavior. This new scientific information also includes a growing number of discoveries in genetics, which have emerged following the sequencing of the human genome. In addition, recent advances in neuroimaging have made it possible to examine events occurring in the healthy and addicted brains of animals and humans, further elucidating the underlying processes. The results of new, large-scale population studies inform much of the epidemiologic coverage of substance use, abuse, and dependence. We have gone to some lengths to reorganize the sections on treatment in as intuitive a way as possible and to include new developments in the use of medications, which increasingly are being combined

with psychosocial interventions in the treatment of individuals with addictive disorders.

Recognizing the cultural importance of how addiction is perceived both in the United States and in societies and political systems throughout the world, the editorial board obtained authoritative essays on such popular subjects as drugs in the movies, the effect of the Internet on drug use, and the coverage of addiction issues in the media. In order to give the reader a broad view of how these issues are understood and dealt with in cultures other than that of the United States, we commissioned articles on drug use and trafficking in a representative group of countries and regions.

We have tried to maintain standards of objectivity in the treatment of controversial subjects and to provide enough information on competing theories and points of view so that readers may draw their own conclusions. One of the main challenges in compiling these volumes was to ensure that the language used by the contributors was not so technical as to make the entries obscure. In reviewing entries prior to publication, a concerted effort was made to use lay language whenever possible and, when technical terms were required, to define them. We, the editors in chief, are satisfied that the finished work provides an authoritative source of information that will help to educate the general public on a variety of complex and controversial issues.

This third edition contains 545 entries, of which nearly 70 percent are either completely new (133 articles) or substantially revised and updated (236 articles). Early on, the editors decided, and Macmillan Reference personnel agreed, that the extensive list of treatment programs included in the fourth volume of the first two editions should be dropped. It was the board's judgment that such a list would fall out of date so fast as to be of little use to the reader.

In early 2006, Kate Hanley of Macmillan Reference invited Pam Korsmeyer and Henry Kranzler to consider sharing the task of editor in chief of a third edition of the *Encyclopedia*. Both were pleased and honored to accept the invitation. Ms. Korsmeyer had worked for many years as an editor and writer on the history of use, abuse, and control of psychoactive substances, and she was happy to be able to reengage the field after several years' absence. Dr. Kranzler has been a clinician and investigator in addictions for more than twenty years and welcomed the opportunity to survey the biological and medical aspects of the field comprehensively, as required by a thorough revision of the *Encyclopedia*.

At the beginning of the *Encyclopedia* project, the editors in chief and the Macmillan Reference project managers agreed that the work of constructing the table of contents, developing "scopes" for each article, and reviewing the finished essays should be divided among six fields of interest. A prominent scholar was then invited to take responsibility for each of the six fields, and the two editors in chief oversaw three fields apiece. Henry Kranzler worked with Deborah Hasin (epidemiology), Kathleen Carroll (treatment), and Michael Kuhar (neuroscience and pharmacology). Pam Korsmeyer guided the efforts of Nancy Campbell (history, society, and culture), Eric Wish (public policy), and Virginia Berridge (international issues). Howard Kushner also participated in the initial development of the table of contents, contributing first-rate work to the coverage of history, society, and culture. When he found that he was unable to remain on the editorial board, Nancy Campbell stepped in, much to the good fortune of the project and the editors.

The substantial organizational effort could not have been possible without the contributions of the staff at Macmillan/Gale, who were ably led by Kate Hanley, Jeffrey Lehman, and Alan Hedblad. Their tireless dedication kept the editorial board and editors in chief focused on the task of identifying suitable authors for the many revised and new entries, providing direction in the preparation of initial draft entries, and thoroughly editing the entries to ensure their suitability for inclusion in the *Encyclopedia*.

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Slang Terms in U.S. Drug Cultures
Sleep, Dreaming, and Drugs
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U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA)
U.S. Government Agencies: U.S. Customs and Border Protection (CBP)
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Complications: Liver (Metabolic)
Complications: Medical and Behavioral Toxicity Overview
Complications: Nutritional
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ABSTINENCE VIOLATION EFFECT (AVE). The abstinence violation effect (AVE) describes an individual's affective and cognitive reaction following a lapse, or initial return to an undesired behavior. When an individual makes a commitment to abstain from or moderate a specific behavior (for example, substance use, eating, or sexual behaviors) and then re-engages in that behavior, the emotional response and cognitive attributions may mediate the potential for a full relapse, or return to the original pattern. The AVE refers to both the affective responses (pleasure, guilt) as well as the cognitive judgments of locus and controllability, which in turn may affect the emotional response. The AVE surfaces primarily when the initial affective response is not pleasant and when the cognitive appraisals support stable, internal traits such as lack of willpower. Whereas any lapse may increase the chance of relapse, lapses mediated by the AVE have an increased probability to lead to full relapse.

In relapse prevention (RP), the goal is to redirect attention and attribution from the internal locus and uncontrollability of the AVE to more external or situational factors that can be anticipated and managed. Essentially, cognitive restructuring may be used to shift attribution from those stable, internal traits to situational or temporary states. RP focuses on identifying high-risk situations, defining alternative coping skills, and altering outcome expectancies. These strategies, combined with more general techniques of stimulus-control and urge-management, reduce the likelihood of a lapse leading to a full relapse. Although the definitions and mechanisms may vary, researchers have found empirical support for the AVE in various behaviors, including addiction to alcohol and drugs, eating disorders, and sexual offenses.

See also **Relapse; Treatment: A History of Treatment in the United States.**

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ABUSE LIABILITY OF DRUGS: TESTING IN HUMANS. There is virtually no drug used to treat illness that does not also pose certain risks. One such risk, generally limited to drugs that have actions on the central nervous system, is that the drug will be misused or abused because of these effects. Drugs such as these are said to have abuse potential or abuse liability. If the drugs have an important therapeutic use that is believed to outweigh the abuse liability, they will probably be made available, but they will be subject to certain legal controls under various federal and state laws. Between the 1960s and the early 2000s, a number of methods were developed to test new drugs to determine their abuse liability, so that both the public and the medical profession could be warned about the need for appropriate caution when using certain drugs. These methods involve preclinical testing in animals and clinical testing in humans.

There are myriad reasons that testing with humans is useful and necessary in the development of safer and more effective pharmacological agents. When research on laboratory animals demonstrates some degree of abuse liability for a specific drug, it must be validated with human research studies. Doing so reduces the likelihood of error in assessing potential risks. Moreover, self-reported changes associated with the subjective effects of medicinal drugs can be more readily evaluated in the humans for whom they were developed. Human clinical studies are also important in determining appropriate dose levels and dosage forms to ensure safety and efficacy while minimizing unwanted side effects. Finally, comprehensive and effective testing with humans helps to determine how best to reduce the availability of drugs that are likely to be abused to those who are likely to misuse them and to provide for the legitimate medical and scientific use of such pharmacological agents.

HUMAN VOLUNTEER SELECTION

One important factor in drug abuse liability testing with humans is the manner in which the volunteer subjects are chosen to participate in the assessment procedures. In most studies, the human volunteer subjects have some experience with drug use, but wide variations exist in the nature and extent of their drug use and abuse. Some studies, for example, use students and other volunteers whose misuse and abuse of drugs has been mostly recreational; other studies involve people with histories of more intensive drug use and abuse over extended periods. Also, the settings in which the tests are conducted vary widely, from residential laboratory environments, where the subjects live for several days or weeks at a time, to laboratories, where the subjects do not remain in residence but continue their daily routine after drug ingestion. Variations also occur in the age of the subjects tested and the time of day that the drug is administered. Often subjects have been selected for specific human drug-abuse-liability tests on the basis of some special features (e.g., anxiety levels, level of alcohol consumption) to determine the extent to which such factors influence the outcome of the tests.

Convincing evidence exists that many of these factors—particularly the subject's prior experience using drugs or alcohol—play an important role in the assessment of abuse liability. The obvious value in using subjects with prior exposure to the drug in question lies in the fact that these individuals are similar to those most likely to misuse drugs with abuse liability—for example, drug abusers who help determine whether a new drug has a greater or lesser chance for abuse than the one they already know. It is also important to carry out abuse liability testing with people who, for example, do not usually abuse drugs but are light social drinkers, to assess the likelihood of abuse (and potential interactions with alcohol) of certain generally available medications, such as sleeping pills or appetite suppressants.

DRUG COMBINATIONS

The prediction of a drug's abuse liability, based on a wide variety of testing procedures with humans, is further complicated by the fact that drugs of abuse are often used in combination with other pharmacological agents. This situation creates some very difficult challenges for the testing of abuse liability because of the large number of possible drug combinations that need to be tested and their unknown, potentially toxic, effects. While it has long been known that drug abusers use drugs simultaneously, such as cocaine and heroin or marijuana and alcohol, few testing procedures have been developed to assess their interactions. Even more puzzling is the fact that some drugs with opposite

effects (e.g.,stimulants such as amphetamines and depressants such as barbiturates) are known to be used simultaneously by polydrug abusers (people who abuse more than one drug at a time), suggesting that unique subjective effects may be important factors in such abuse patterns.

PRINCIPLES OF ABUSE LIABILITY TESTING

Based on extensive research undertaken between about 1970 and the early 2000s, some important general principles governing abuse liability testing with humans were established. First, a meaningful assessment requires that the test drug be compared with a drug of known abuse liability to provide a standard for evaluation. Second, the assessment procedure must involve the indicated comparison over a range of doses of both the test drug and the standard drug of abuse. This principle permits both a quantitative and a qualitative comparison of the drugs, while guarding against the possibility of overlooking some unique high- or low-dose effects. Third, the testing procedures should include measures of drug effects in addition to those found in the laboratory, which directly predict the likelihood of abuse. With these additional measures, it is often possible to obtain reliable estimates of abuse liability by comparing test drugs with a drug of abuse across a range of effects as a standard for evaluation. Fourth, confidence in conclusions regarding the abuse liability of a drug can be enhanced by utilizing a range of measures and experimental procedures. This is because the present level of knowledge in this area does not permit a firm determination of the best or most valid predictor of the likelihood of abuse. Finally, a population of test subjects with a history of drug use appears to be the most appropriate selection for predicting the likelihood of abuse of a new test drug, since this is the population who might use such a drug in that way.

DEVELOPMENT OF ABUSE LIABILITY TESTING PROCEDURES

Since the mid-nineteenth century, literary accounts of the use and misuse of opium, marijuana, and cocaine, among other substances, have emphasized their mood-altering effects and their potential for abuse. Only in more modern times, however, have systematic methods for measuring such subjective effects been refined through the use of standardized questionnaires. When volunteers who are experienced drug users complete questionnaires after they have taken a drug, their answers to the subjective-effects questions—how they feel, their likes and dislikes—readily distinguish between the various drugs and doses, as well as between the presence of the drug or its absence (i.e., placebo).

This basic subjective-effects methodology has been further refined by using a training procedure to ensure that the human volunteer can differentiate a given drug (e.g., morphine) from a placebo (i.e., non-drug). New drugs are then tested to evaluate their similarity to the trained reference drug of abuse. This behavioral drug discrimination method permits the volunteer to compare a wide range of subjective and objective effects of abused drugs with those of new drugs. These procedures have proven to be highly reliable and, therefore, very useful in identifying drugs with potential abuse liability.

Among the most important factors in assessing abuse liability is the determination of whether humans will take the drug when it is offered to them and whether such drug taking is injurious to the individual or society. These cardinal signs of drug abuse have provided an important focus for laboratory animal self-injection experiments, but systematic studies in which humans self-administer drugs of abuse have been less common. Methods have been developed with humans, however, for comparing the behavioral and physiological changes produced by self-administration of a known drug of abuse with the changes produced by other self-administered drugs. In addition to the questionnaires, physiological measures—such as changes in heart rate, blood pressure, changes in the blood or different types of tissue, levels of systemic arousal, and other, more sophisticated physiological measures such as CT scans, MRIs, functional MRIs, and the like—are used to make comparisons between subjective sensation and bodily changes associated with abuse liability. Changes in brain chemistry and cortical arousal can be potent indicators of abuse potential.

The measure that has proven most useful in this approach to human drug abuse liability assessment is the ability of a drug to reinforce and maintain self-administration behaviors much like the behaviors used to obtain food and water. Such reinforcing effects of drugs are an important determinant influencing the

likelihood that a particular drug will be abused. Laboratory studies with volunteers who are experienced drug users, for example, have shown that they will perform bicycle riding exercises to obtain doses of abused drugs (e.g., pentobarbital). There is a systematic relationship between the amount of exercise performed and the amount of drug available (i.e., higher doses and shorter intervals between doses produce more exercise behavior than lower doses and longer interdose intervals). When a placebo or a drug that is not abused (e.g., chlorpromazine) is made available for bicycle riding, by contrast, the rate of self-administration declines to near zero.

Differences between drugs in abuse liability can also be assessed by determining whether humans prefer one drug of abuse to another. During a training period, for example, experienced drug users sample coded capsules containing different drugs or different doses of a drug. Then, during subsequent test sessions, they are presented with the coded capsules and allowed to choose the one containing the drug or drug dose they prefer. This blind procedure (i.e., the volunteers are not told what drugs the capsules contain) prevents biases that might be introduced by using the drug names. When neither the volunteer subject nor the person conducting the test knows what drug the capsules contain, the procedure is referred to as *double-blind*.

Not surprisingly, it has also been shown that the preference for one drug over another or one drug dose over another agrees well with ratings of drug-liking made independently of the choice tests just described. In self-administration studies in which volunteers show a preference for one drug of abuse over another, subjective ratings of liking and positive mood changes were clearly more frequent for the preferred drug than for the drug chosen less often. Such self-reports have inherent limitations, however, because of variations in individual verbal skills, which make it necessary to confirm such findings with other measures.

In addition to the self-administration and subjective-effects measures that are of obvious value in testing the abuse liability of drugs in humans, other quantitative drug effect measurements have proven useful. When, for example, observer ratings (e.g., nurses watching the patients) and performance tests (e.g., speed of movement) are measured after different drugs are administered to volunteers, the results can be compared to determine whether the behavioral changes produced by a test drug are the same as or different from those of a known drug of abuse. When a number of different performance tests (e.g., arithmetic calculations, memory for numbers and letters, speed of reaction) are given following such drug administration, it is possible to construct a behavioral profile showing the performance effects of different drugs. Comparisons between different drugs and test drugs with regard to the similarity of such profiles across their respective dose ranges increase confidence in assessments made of the abuse liability of unknown drugs.

EFFECTIVENESS OF ABUSE LIABILITY TESTING

Given the availability of procedures for abuse liability testing in humans it is reasonable to ask how well they work. That is, it is worth asking if it has been possible to predict from the results of these tests whether a new drug will be abused when it becomes generally available. The two major sources available for checking the effectiveness of human abuse liability testing procedures are case reports by clinicians of patient drug abuse and epidemiological surveys of large numbers of individuals as well as of specific target sites (e.g., hospital emergency rooms). Both of these approaches have shortcomings, as they lack the precision and focus that human laboratory testing can provide. Despite the drawbacks, they can detect abuse liability problems in both specific groups of individuals and the population at large, in a manner that has generally validated the results of human laboratory testing procedures.

ETHICAL CONSIDERATIONS

Several codes and regulations agreed on by scientists, regulatory bodies such as federal agencies, and the lay public provide norms for the conduct of research and testing with human volunteers. In general, they require a clear statement, understandable to the volunteer, of the risks and benefits of the testing procedure, as well as an explicit consent document in written form. After it is clear that the participant thoroughly appreciates all that is involved and the potential consequences of participation, the volunteer signs the consent form in the presence of a witness who is not associated with the

research. These required procedures ensure both the autonomy and the protection of volunteers for drug abuse liability testing.

See also **Abuse Liability of Therapeutic Drugs: Testing in Animals; Controlled Substances Act of 1970; Reinforcement; Research, Animal Model: An Overview.**

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ABUSE LIABILITY OF THERAPEUTIC DRUGS: TESTING IN ANIMALS.

Determining the probability that a new drug will be abused is an important step in reducing the overall abuse of therapeutic drugs. Since the likelihood that a drug will be abused by a patient must be carefully weighed against the benefit provided by the drug, it is important that research outline any and all reinforcing effects a drug may have which could lead to subsequent abuse. Prediction of the likelihood of abuse has historically been based upon human experiments and observation. This method, however, is increasingly being replaced with experimentation on animals.

Research conducted since the early 1960s has shown that animals such as monkeys and rats will, with very few exceptions, repeatedly self-administer the same drugs that human beings are likely to abuse. Moreover, test animals do not self-administer drugs that human beings do not abuse.

Research based on animal testing is conducted in a slightly different manner and often requires laboratory procedures not needed for research based on human test subjects. Provisions must be

made to allow the animal a means by which to self-administer the drug. Since animals frequently are not physically able to administer a drug in the same way a human would, alternate methods are employed. Animals may be taught to push levers or do similar actions in order to get a dose of a drug. The results of these drug self-administration studies in animals play a critical role in the prediction of the likelihood of abuse of new drugs in human beings.

The liability that a drug will be abused is often evaluated by what has been termed a "substitution procedure." Such research begins with the administration of a known drug, which is then substituted with a new drug under investigation. The first phase in the substitution procedure is designed to establish a baseline of how much effort an animal is willing to make to obtain a drug dose in general. Each day an animal is allowed to give itself a drug of known potential for abuse. The researcher notes how frequently the animal takes a dose and how much effort it is willing to make to get a dose of the drug. The researcher can make a lever harder to push, make the animal push it repeatedly, or make the animal follow a complicated set of actions to get a dose. This provides a baseline against which to compare the effects of the new drug which will be studied.

For example, a monkey may give itself cocaine or codeine via intravenous injections during sessions that last several hours. When session-to-session intake of the known drug is stable (that is, stays about the same, thus showing the dosage which is sufficient to satisfy the animal and reduce its drive to obtain more), the liquid in which it was dissolved is substituted for the baseline drug for several consecutive sessions. Since this liquid is usually neutral, with no positive or negative effects, the animal gives itself fewer and fewer injections until it hardly bothers pushing the lever at all. The animal is briefly returned to baseline conditions, followed by a substitution period during which a dose of the test drug is made available. This continues for at least as many sessions as were required for the animal to stop bothering with pushing the lever for the neutral liquid. This process is repeated with different concentrations of the new drug until the experimenter has tested a range of possible doses of the new medicine.

The rates at which the animal gives itself the test drug, neutral liquid, and known addictive drug are then compared. A new drug that the animal prefers to the neutral liquid is considered to be a substance that reinforces the desire for itself (a "positive reinforcer") and would thus be predicted to have abuse liability.

Such substitution procedures provide information which indicates whether or not a drug is liable to be abused, but do not allow a comparative estimate as to whether or not a new drug is more addictive or less addictive than other known drugs. These procedures measure how frequently the animal gives itself a dose, a measure that reflects both the direct effects of the drug and the effects of the drug's reinforcement of the desire for itself. Another method must be used to measure the reinforcing effect of a drug separately from its other effects. To compare drugs, it is useful to know how big the maximum reinforcing effect is—termed its *reinforcing efficacy*. Several procedures have been developed to measure reinforcing efficacy. Most either allow an animal to choose between the new drug and another drug or non-drug reinforcer (choice procedures), or they measure how hard an animal will work to obtain an injection (progressive-ratio procedures).

In choice procedures, the measure of reinforcing efficacy is how often the new drug is chosen in preference to the other drug (or non-drug). In progressive-ratio procedures, the number of times the animal must push the lever in order to get a drug injection is increased until the animal no longer bothers to push the lever. At some point the animal determines that it is not worth the extra effort to get another dose. This point is called the break point and is a measure of the reinforcing efficacy of the drug.

The fact that animals given a choice between different strengths of the same drug show a propensity to choose the higher dose most often is evidence that these procedures provide a valid measure of reinforcing efficacy. In addition, break points are higher in progressive-ratio experiments involving higher stable doses and lower for experiments involving lower doses. Results of both the choice and the progressive-ratio procedures in animal research are consistent with what is known about abuse of drugs in human

beings—that is, drugs such as cocaine, a highly preferred drug in choice studies, maintain higher break points in progressive-ratio studies than other drugs, and are frequently abused.

These experiments show how animals discriminate among drugs, and the extent to which they prefer certain drugs over other drugs. The results may be used to predict potential subjective effects in human beings. Since subjective effects play a major role in drug abuse, such experiments are an important tool used in the evaluation of the likelihood of abuse in new drugs. A new drug with subjective effects similar to those of a known, addictive, and often abused drug is likely to be abused itself. Additionally, drug-discrimination experiments not only identify the potential for abuse but also provide important information which allows researchers to classify new drugs based on their predicted subjective effects, something that drug self-administration experiments cannot do. Thus, drug discrimination provides additional information relevant to the comparison between the new drug and drugs that we already know are addictive and frequently abused. For example, a monkey shows a similar discrimination pattern using a new drug as it has shown previously using a known drug such as cocaine. This new drug is likely to be abused and to have subjective effects similar to those produced by cocaine.

ABUSE LIABILITY OF THERAPEUTIC DRUGS: TESTING IN ANIMALS: CONCLUSION

Researchers have improved methods for predicting the likelihood that a new drug will be abused. Using animals in substitution, choice, and progressive-ratio procedures has greatly enhanced researchers' understanding of factors involved in determining the liability that a new drug or chemical compound will be abused. Current research techniques allow the evaluation of likely preference and the reinforcing efficacy of a new compound based on experiments with animals such as monkeys and rats. This information is then used to reliably predict whether a drug is likely to be abused and to which known drugs it is likely to be similar, both in terms of how addictive it is and what its subjective effects will be. Such information is clearly valuable in deciding how much to restrict a new drug and is a critical tool in the effort to reduce the abuse of therapeutic drugs.

See also **Abuse Liability of Drugs: Testing in Humans; Controlled Substances Act of 1970; Reinforcement; Research, Animal Model: An Overview.**

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ACAMPROSATE.

See **Treatment, Pharmacological Approaches to: Acamprosate.**

ACCIDENTS AND INJURIES FROM ALCOHOL.

Trauma (bodily injury) is a major social and medical problem in both developed and developing countries. Injuries are among the leading cause of death and disability in the world, and affect all populations, regardless of age, sex, income, or geographic region. In 1998 about 5.8 million people died of injuries worldwide, and injuries caused 16 percent of the global burden of disease (Krug et al., 2000). In developed countries injuries are the leading cause of death between the ages of one and forty, and in the United States population injuries are the fourth leading cause of death (exceeded only by heart disease, stroke, and cancer). Of all deaths from injury in the United States, about 65 percent are classified as "unintentional" (which excludes deaths from suicide and homicide). Unintentional injury is the leading cause of death in the United States among those under forty-four years of age. More than a hundred

	BAC = .00		BAC = .01–.07		BAC = .08+			Total fatalities in alcohol-related crashes	
Year	Number	Percent	Number	Percent	Number	Percent	Total number	Number	Percent
1994	23,409	57	2,322	6	14,985	37	40,716	17,308	43
1995	24,085	58	2,490	6	15,242	36	41,817	17,732	42
1996	24,316	58	2,486	6	15,263	36	42,065	17,749	42
1997	25,302	60	2,290	5	14,421	34	42,013	16,711	40
1998	24,828	60	2,465	6	14,207	34	41,501	16,673	40
1999	25,145	60	2,321	6	14,250	34	41,717	16,572	40
2000	24,565	59	2,511	6	14,870	35	41,945	17,380	41
2001	24,796	59	2,542	6	14,858	35	42,196	17,400	41
2002	25,481	59	2,432	6	15,093	35	43,005	17,524	41
2003	25,779	60	2,427	6	14,678	34	42,884	17,105	40
2004	25,918	61	2,325	5	14,593	34	42,836	16,919	39
2005	25,920	60	2,489	6	15,102	35	43,510	17,590	40
2006	25,040	59	2,480	6	15,121	35	42,642	17,602	41

SOURCE: National Highway Traffic Safety Administration Fatality Analysis Reporting System, U.S. Department of Transportation.

Table 1. Alcohol content and alcohol-related accidents, 1994–2006. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

thousand Americans die annually as a result of accidental injuries, nearly half of which are from motor vehicle crashes, and the remainder from falls, burns, poisonings, and drownings, among other causes. Unintentional injury accounts for an even higher rate of morbidity, with the rate of serious injury estimated to be over three hundred times the mortality rate (Vyrostek et al., 2004), and it is estimated that more than seventy million Americans annually require medical treatment for non-fatal unintentional injuries. Intentional injuries, those resulting from violence-related events (homicides and assaults) and from suicide (attempted and completed), also account for substantial proportions of fatalities and of those requiring medical intervention.

Globally, alcohol is among the most important risk factors for both morbidity-related disability and mortality. Injuries constitute 46 percent of the deaths attributable to alcohol and 42 percent of the Disability-Adjusted Life Years (DALYs) (Rehm et al., 2004), with unintentional injuries accounting for over twice the DALYs as intentional injuries. The problem of alcohol-related injuries is particularly alarming in many developing countries, where alcohol consumption is rapidly increasing, injury rates are extremely high, and appropriate public policies have not been implemented.

The first documentation of alcohol's involvement in injury dates to 1500 BCE, with an Egyptian papyrus warning that excessive drinking leads to falls and broken bones. The scientific study of alcohol and injuries was the subject of much investigation throughout the twentieth century. Data from both coroner and emergency room (ER) studies indicate that a large proportion of victims of both fatal and nonfatal injuries test positive for blood alcohol—this proportion is greater than one would expect to find in the general population on any given day. The consumption of alcohol has been highly associated with fatalities and serious injuries, but whether or not alcohol is more common in injuries of greater severity has been an issue of ongoing debate (Li et al., 1997). Alcohol may be significantly associated with increased risk of serious injury, possibly due to other factors that are associated with alcohol use, such as speeding, not wearing seat belts or helmets, and other risk-taking behaviors. Studies of alcohol, injury, and risk-taking dispositions in the general population have shown risk-taking, impulsivity, and sensation-seeking to be associated with both injury occurrence and alcohol consumption (Cherpitel, 1999). However, alcohol intoxication itself can bias injury severity scores upward, and those more severely injured are also more likely to reach the ER sooner, and consequently more likely to have a positive (and higher) blood alcohol concentration (BAC) than those less severely injured who arrive later.

Although alcohol cannot be said to cause the accident in most cases, alcohol consumption is thought to contribute to both fatal and nonfatal injury occurrence, primarily because it is known to diminish motor coordination and balance and to

	Male			Female		
		Percent			Percent	
Year	Total	BAC = .01+	BAC = .08+	Total	BAC = .01+	BAC = .08+
1994	40,233	30	26	13,567	17	14
1995	41,235	30	25	14,184	16	13
1996	41,376	29	25	14,850	16	13
1997	40,954	28	24	14,954	15	12
1998	40,816	28	23	15,089	15	12
1999	41,012	28	23	14,835	14	12
2000	41,795	29	24	14,790	16	13
2001	41,901	29	24	14,919	15	13
2002	42,377	29	25	14,999	15	12
2003	42,586	28	24	15,211	14	12
2004	42,250	28	24	15,384	15	12
2005	43,282	28	24	15,059	16	13
2006	41,975	28	24	14,655	18	15

SOURCE: National Highway Traffic Safety Administration Fatality Analysis Reporting System, U.S. Department of Transportation.

Table 2. Fatal accidents by sex and blood alcohol concentration, 1994–2006.
ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

impair attention, perception, and judgment with regard to behavior, placing the drinker at a higher risk of accidental injury than the nondrinker. The residual or hangover effects of alcohol consumption may also contribute to injury occurrence. It should not be overlooked that the use of alcohol in combination with other drugs may potentiate the effects of alcohol and increase the risk of injury.

ESTIMATES OF ALCOHOL'S INVOLVEMENT

In U.S. studies, the proportion of injured patients testing positive for estimated BAC at the time of admission to the ER has ranged from 7 percent to 22 percent, while data from other countries show ranges from 4 percent (Canada and the Czech Republic) to 59 percent (South Africa) (Cherpitel, 2007). Reviews of these studies suggest that the variation in BAC may be due to differences in the time that elapsed between the injury and arrival in the ER, as well as to individual characteristics of the particular ER populations studied (such as age, sex, and socioeconomic status—all known to be associated with alcohol consumption in the general population), and also to the mix of various types of injury in the ER caseload (Cherpitel, 1993). For example, alcohol consumption is more commonly associated with injuries resulting from violence than from any other cause. In studies that have been restricted to weekend evenings, when one would expect a large proportion of the population to be consuming alcohol, the proportion of those testing positive for alcohol at the time of ER admission was particularly high. In coroner studies, such as those conducted by Haberman and Baden (1978), alcohol-related fatalities were estimated to account for about 43 percent of all unintentional injuries. Studies that have compared estimated BAC between fatal and nonfatal injuries in the same geographic locality have shown higher rates of positive BACs among fatal injuries (57%) than nonfatal injuries (15%) (Cherpitel, 1996). It is well known that many who drink also consume other psychoactive drugs, so it is not possible to ascertain the independent effect of alcohol on both fatal and nonfatal accidents.

TRAUMA RELATED TO MOTOR VEHICLES

Motor Vehicle Accidents. Motor vehicle accidents are the leading cause of death from injury—and the greatest single cause of all deaths for those between the ages of fifteen and thirty-four in the United States. Almost 50 percent of these fatalities are believed to be alcohol related, and alcohol's involvement is greater for drivers in single-vehicle nighttime fatal crashes (U.S. Department of Health and Human Services, 1997). The risk of a fatal crash is estimated to be from three to fifteen times higher for those with a BAC of at least 0.10 percent (100 milligrams of alcohol per 100 milliliters of blood), than for drivers with a zero BAC (Roizen, 1982). Alcohol is more frequently present in fatal

than in nonfatal crashes. It is estimated that 25 percent to 35 percent of drivers requiring ER care for injuries resulting from such crashes have a BAC of 0.10 percent or greater.

Motorcycle Accidents. Motorcyclists are at a greater risk of death than automobile occupants, and it has been estimated that up to 50 percent of fatally injured motorcyclists have a BAC of at least 0.10 percent (Romelsjö, 1995).

Pedestrian Accidents. Pedestrians killed or injured by motor vehicles are also more likely to have been drinking than those not involved in such accidents (Romelsjö, 1995). It is estimated that 31 percent to 44 percent of fatal injuries to pedestrians are due to alcohol intoxication, with 14 percent of the fatal pedestrian accidents involving an intoxicated driver and 24 percent involving an intoxicated pedestrian.

Aviation Accidents. Flying skills are impaired at BACs as low as 0.025 percent, and a BAC of 0.015 percent or greater has been found in 18 percent to 43 percent of pilots deceased from accidents (Romelsjö, 1995).

HOME ACCIDENTS

Among all nonfatal injuries occurring in the home, an estimated 22 percent to 30 percent involve alcohol, with 10 percent of those injured having BACs of over 0.10 percent at the time of the accident. Coroner data suggest that alcohol consumption immediately before a fatal accident occurs more often in deaths from falls and fires than in motor vehicle deaths.

Falls. Falls are the most common cause of nonfatal injuries in the United States (accounting for over 60%) and the second leading cause of fatal accidents (Baker et al., 1992). Alcohol's involvement in fatal falls has been found to range from 21 percent to 77 percent, and in nonfatal falls from 17 percent to 57 percent. Alcohol may increase the likelihood of a fall as much as sixty times in those with high BACs, compared with those having no alcohol exposure.

Fires and Burns. Fires and burns are the fourth leading cause of accidental death in the United States (Baker et al., 1992). Alcohol involvement has been estimated in 12 percent to 83 percent of these fatalities (with a median value of 46%), and up to 50 percent of nonfatal burn injuries (with a median value of 17%). In a review of studies of burn victims, Hingson and Howland (1993) estimated that about 50 percent of burn fatalities were attributed to intoxicated individuals and that alcohol exposure was most frequent among victims of fires caused by cigarettes.

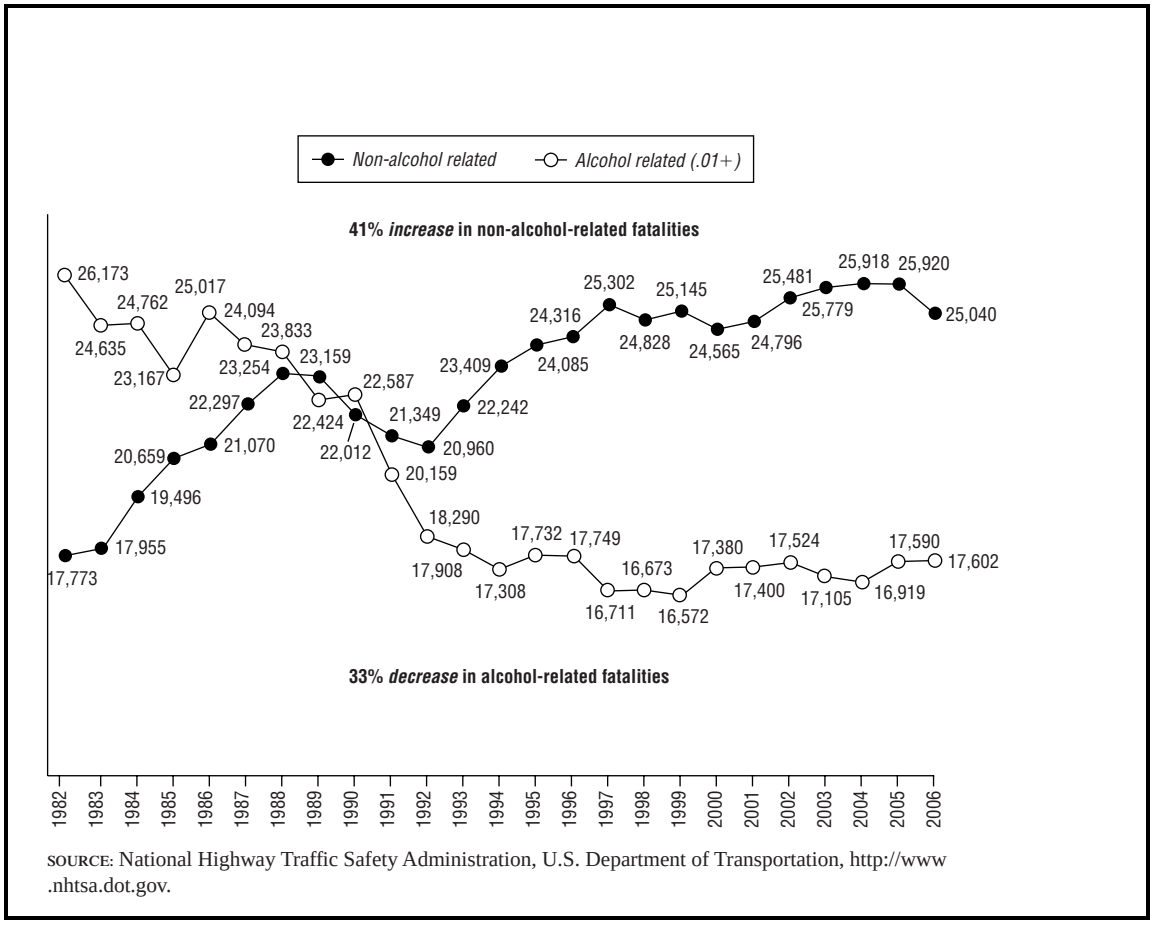
RECREATIONAL ACCIDENTS

Drownings. Drownings rank as the third leading cause of accidental death in the United States for those aged five to forty-four, and the fourth leading cause across all age groups (Howland et al., 1995). Haberman and Baden (1978) reported that 68 percent of drowning victims had been drinking, but other estimates have ranged from 30 percent to 54 percent (with an average of 38%) (Hingson & Howland, 1993). Alcohol is consumed in relatively large quantities by many of those involved in water-recreation (especially boating) activities, and studies suggest that those involved in aquatic accidents are more likely to be intoxicated than those not involved in such accidents. In a review of the literature on those who came close to drowning, Roizen (1982) found that about 35 percent had been drinking at the time.

Bicycle Injuries. Bicycling is the leading cause of recreational injuries, resulting in over 500,000 ER visits, 20,000 hospitalizations and 1,000 deaths annually in the United States (Li et al., 1996). Among those fatally injured, 32 percent have been found to be BAC positive and 23% had BACs of 0.01 percent or above. A comparison of fatal bicycle injuries with non-fatal injuries found fatal injuries more likely to have positive BACs (30% vs. 16%) and to have BACs of 0.10 percent and above (22% vs. 13%) (Li et al., 1996).

Snowmobiles and Mopeds. Forty percent of snowmobile injuries (Smith & Kraus, 1988) and 30 percent of moped injuries (Roizen, 1989) were found to involve alcohol.

Hypothermia and Frostbite. Alcohol has been found greatly to increase the risk of hypothermia and frostbite. Among exposure-related fatalities, 63 percent were found to be BAC positive, with 48



SOURCE: National Highway Traffic Safety Administration, U.S. Department of Transportation, http://www.nhtsa.dot.gov.

Figure 1. Crash fatalities by alcohol involvement. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

percent at 0.15 percent or higher (Luke & Levy, 1982), while 53 percent of frostbite patients have been found to be alcohol positive (Urschel, 1990).

WORK-RELATED ACCIDENTS

Alcohol's involvement in work-related accidents varies greatly by type of industry, but the proportion of those testing positive for blood alcohol following a work-related accident is considerably lower than for other kinds of injuries, particularly in the United States, since drinking on the job is not a widespread or regular activity. Among work-related fatalities, an estimated 15 percent were positive for blood alcohol, and a range of 1 percent to 16 percent has been estimated for nonfatal injuries (Roizen, 1989; Stallones & Kraus, 1993).

INTENTIONAL INJURIES

Violence-Related Injuries. Both fatal and nonfatal injuries commonly result from violence, and these injuries are more likely to be alcohol-related than injuries from any other cause, for both men and for women, regardless of age. Such injuries are considered intentional and include those nonfatal injuries resulting from assaults and fights, as well as fatal injuries from homicides. Alcohol is more likely to be involved in fatal injuries from violence than in nonfatal injuries treated in an ER in the same geographic locality (Cherpitel, 1996). A review of ER studies showed that between 22 percent and 70 percent of violence-related injuries were BAC positive, compared to 7 percent to 22 percent of non-violence-related injuries attending the same ERs during the same period of time (Cherpitel, 1994). These figures refer to alcohol involvement among the victims of violence-related events, and less is known about alcohol involvement of the perpetrator of such events, but the correlation is thought to also be high. ER patients with violence-related injuries are also more likely to be heavier drinkers and to report alcohol-related problems than those with injuries from other causes.

Suicide. A review of suicides found a range of 10 percent to 69 percent for alcohol positive cases among completed suicides (with an average of 33%) and a range of 10 percent to 73 percent for alcohol positive cases among attempted suicides (Cherpitel et al., 2004). About 20 percent of suicide victims have been identified as alcohol dependent, and are at increased risk of suicide compared to those in the general population. The suicide risk among alcoholics is estimated to be almost twice as high as for non-alcoholics.

ALCOHOLISM, VOLUME OF DRINKING, AND DRINKING PATTERN

The available literature on the role of alcoholism in injury occurrence suggests that problem drinkers and those diagnosed as alcoholics are at a greater risk of both fatal and nonfatal injuries than those in the general population who may drink prior to an accident. Alcoholics and problem drinkers are significantly more likely to be drinking, and to be drinking heavily, prior to an accident than others. Haberman and Baden (1978) found that among fatalities from all causes, alcoholics and heavy drinkers were more than twice as likely as non-problem drinkers to have a BAC of 0.10 percent or above. Alcoholics have also been found to experience higher rates of both fatal and nonfatal accidents, even when sober. Analysis of national mortality data found that those who died of injury drank more frequently and more heavily than those who died of disease, and that daily drinking, binge drinking (consuming five or more drinks per occasion), and heavier drinking (fourteen or more drinks per week) increased the likelihood of injury as the underlying cause of death (Li et al., 1994). Chronic alcohol abuse has long-term physiological and neurological effects that may increase the risk of accidents. Chronic drinking also impairs liver function, which plays an important part in injury recovery. Heavy drinking also compromises the immune system, predisposing the alcoholic to bacterial infections following injury. The risk of accidental death has been estimated to be from three to sixteen times greater for alcoholics than for non-alcoholics, with the highest risk being death from fires and burns. Haberman and Baden (1978) found that among all fatalities from fires, 34 percent involved alcoholics.

A *dose-response relationship* may also be important in risk of injury; that is, the more alcohol consumed, the greater the likelihood of injury occurrence. Reviews of fatal vehicular crashes have found that risk increases exponentially with increasing BAC (Perrine et al., 1989), and a summary of U.S. findings show a dose-response relationship, with a BAC of 0.08 percent, 0.10 percent, 0.15 percent and 0.20 percent associated with a twofold, sevenfold, tenfold, and twentyfold increased risk, respectively, for a road traffic accident (Brismar & Bergman, 1998). A Finnish ER study also found a dose-response relationship between BAC and the likelihood of injury from falls, with those having BACs between 0.06 percent and 0.10 percent being three times more likely to be injured than those with non-detectable blood alcohol; while those with BACs between 0.10 percent and 0.15 percent were ten times more likely, and those with BACs over 0.15 percent were sixty times more likely to have suffered a fall injury (Honkanen et al., 1983).

Although the amount of drinking on any particular occasion is an important risk factor in injury occurrence, the pattern of usual drinking may also play a part in risk of injury. Data from the U.S. general population found the risk of injury increased with an average of one drink a day for both men and women, regardless of age. The risk of injury also increased with the frequency of consuming five or more drinks a day more often than twice a year (Cherpitel et al., 1995). A study of crash-involved drivers showed more frequent drinkers to be at lower risk than less frequent drinkers at all BAC levels (Hurst et al., 1994). Other analysis of drinking and driving in the United States, however, found that the highest risk of injury was associated with those who only occasionally drank heavily, but who drank more than their usual amounts at the time of the event (Gruenewald et al., 1996), suggesting that heavy episodic drinking may be more strongly related to injury than usual volume of drinking. This is supported by data from an ER study showing that those who usually drank little but on occasion drank heavily were at greater risk for injury (Gmel et al., 2006).

See also **Driving, Alcohol, and Drugs; Driving Under the Influence (DUI); Industry and Workplace, Drug Use in; Social Costs of Alcohol and Drug Abuse.**

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CHERYL J. CHERPITEL

ACCIDENTS AND INJURIES FROM DRUGS.

CENTRAL NERVOUS SYSTEM EFFECTS

The effects of drugs, including alcohol, may be divided into three categories: acute, carryover, and chronic. Acute effects are those that occur while the person is directly under the immediate effects of the drug (intoxicated or high), and it is during these times that individuals become very vulnerable to accidents and injuries. Carryover effects are effects that occur after the drug has been essentially eliminated from the system, but the effects of the drugs remain to some degree. A hangover from alcohol use is an example of a carryover effect. Even low dose use can have carryover effects. A seminal study on the ability of airplane pilots to successfully land their aircraft after smoking a single marijuana cigarette showed that 8 and even 24 hours after smoking the marijuana, the ability of pilots to safely land their aircraft was measurably diminished. In each instance of carryover effect, the alcohol or drug has dissipated from the system but clarity of thought, decision-making, and attentiveness may be negatively affected, often in more subtle but equally impacting ways. Chronic effects generally are those advanced medical problems that result from continued intermittent or intensive use of drugs.

Accidents and injuries associated with drug and alcohol use generally occur during the acute or carryover phases of drug use because the conditions that cause the accidents are often due to limited mobility and depth perception, slow reaction time, unawareness of setting, and limited ability to make decisions. Most accidents from drugs and alcohol occur either on the highway or at work.

HIGHWAY ACCIDENTS

According to Car-Accidents.com, there were nearly 6,420,000 auto accidents in the United States in 2005. The financial cost of these crashes was more than $230 billion, with 2.9 million people injured and 42,636 people killed. About 115 people die every day in vehicle crashes in the United States, one death every 13 minutes.

Alcohol. According to the Centers for Disease Control (CDC), during 2005, 16,885 people in the United States died in alcohol-related motor vehicle crashes, representing 39 percent of all traffic-related deaths. In 2005, nearly 1.4 million drivers were arrested for driving under the influence of alcohol or narcotics. Drugs other than alcohol (e.g., marijuana and cocaine) were involved in about 18 percent of motor vehicle driver deaths. These other drugs are generally used in combination with alcohol.

In 2006, the National Highway Transportation Safety Administration (NHTSA) reported that there were 16,005 people killed in the United States in alcohol-related motor vehicle traffic crashes (with individuals having a blood alcohol concentration [BAC] of .01 or higher) and 13,470 fatalities in crashes involving an alcohol-impaired driver (BAC of .08 or higher). These 13,470 alcohol-impaired-driving fatalities in 2006 numbered just slightly more than the 13,451 alcohol-impaired-driving fatalities reported in 1996.

The NHTSA report also noted that the 13,470 fatalities in alcohol-impaired-driving crashes during 2006 represent an average of one alcohol-impaired-driving fatality every 39 minutes and that the rate of alcohol impairment among drivers involved in fatal crashes was four times higher at night than during the day. Other highlights of the report are given below:

The percentage of drivers with a BAC of .08 or above in fatal crashes was highest for motorcycle operators (27%), followed by drivers of light trucks (24%), and then passenger cars (23%). The percentage of drivers with

BACs of .08 or higher in fatal crashes was the lowest for large trucks (1%).

In fatal crashes in 2006, the highest percentage of drivers with a BAC of .08 or higher was for drivers ages 21 to 24 (33%), followed by ages 25 to 34 (29%) and 35 to 44 (25%).

Drivers with a BAC of .08 or higher involved in fatal crashes were eight times more likely to have a prior conviction for driving while impaired (DWI) than were drivers with no alcohol (8% and 1%, respectively).

In 2006, more than 8,200 (55%) of the drivers involved in fatal crashes who had been drinking had a BAC of .15 or greater.

Both females and males had significantly higher death rates in fatal crashes in which the BAC was .08 or greater, 83 percent and 86 percent, respectively.

According to the Insurance Institute for Highway Safety, alcohol involvement is much lower in crashes involving nonfatal injuries, and it is lower still in crashes that do not involve injuries at all.

These results occurred through several years when there was a declining rate of alcohol-related accidents in the United States.

A 2003 report by the National Center for Statistics and Analysis estimated that of the approximately 3 million people who were injured on U.S. public roads, about 250,000 were involved in alcohol-related crashes. Over 60 percent of those injured were vehicle drivers, 30 percent were vehicle passengers, 3 percent involved motorcycles, and 5 percent included non-occupants (pedestrians and others). While estimates vary, according to David Hanson (2008), between 2 and 3 percent of these injury-producing crashes involve intoxicated drivers.

Drugs. Until the late 1990s, there was little investigation into the impact of drugged drivers on highway accidents. Most of the focus on highway accidents and substance abuse pertained to alcohol use. In the early 2000s, however, studies increasingly showed that an unexpected percentage of highway accidents are caused by drugged driving, that is, driving under the influence of drugs other than alcohol. Some studies have shown that many drivers who test positive for alcohol also test positive for the psychoactive chemical in cannabis (THC), making it clear that consuming alcohol and using other drugs are often linked behaviors that combine to affect people's driving.

The Institute for Behavior and Health (IBH) has studied extensively the impact of drug use on highway accidents, and it reports that "Drugged Driving [is a] leading cause of traffic accidents, injuries, and fatalities." Its report cites the following:

10.2 million Americans drove under the influence of drugs in 2006. This corresponds to 4.2 percent of the population aged 12 or older, similar to the rate in 2005 (4.3%), but lower than the rate in 2002 (4.7%). In 2006, the rate was highest among young adults aged 18 to 25 (13%).

Drugged driving causes $33 billion in damages every year based on estimates by the American Automobile Association and IBH.

In any two week period, 1 out of 3 high school seniors has driven after using drugs or ridden with someone who was.

8,600 people died in 2005 as a result of drugged driving.

20 percent of motor vehicle accidents are attributable to drugged driving.

580,000 people were injured in car crashes as a result of drugged driving.

A study by Walsh and colleagues (2004) indicated that 34 percent of motor vehicle crash victims admitted to a Maryland trauma center tested positive for "drugs only"; about 16 percent tested positive for "alcohol only." Approximately 9.9 percent (or 1 in 10) tested positive for alcohol and drugs, and within this group, 50 percent were younger than age 18.

In a large study of almost 3,400 fatally injured drivers from three Australian states (Victoria, New South Wales, and Western Australia) between 1990 and 1999, Drummer and colleagues determined that drugs other than alcohol were present in 26.7 percent of the cases (Drummer et al., 2003). Almost 10 percent of the cases involved both alcohol and drugs.

ACCIDENTS IN THE HOME

An estimated 22 to 30 percent of all nonfatal injuries that occur in the home involve alcohol. One U.S. study showed that people with medically identified alcohol problems had an elevated risk of injury and that 46 percent of problem drinkers required

treatment for at least one injury in a three-year period compared to 38 percent of controls without alcohol problems (Miller et al., 2001). In addition alcohol users sustained an average of two injuries over a three-year period compared to 1.6 injuries for controls. Subjects with a combined alcohol and drug problem had a much higher risk of injury. Women problem drinkers over the age of twenty had a significantly higher risk of injury compared to controls, and by the age of fifty female injury rates exceeded male rates. However, there exists only a modest amount of comprehensive research in the United States on this subject, and where it exists, it almost always relates only to alcohol-related home accidents. Falls are the most common cause of nonfatal injuries in the United States, accounting for over 60 percent and the second-leading cause of fatal accidents. Alcohol is involved in 21 to 48 percent of fatal falls and 17 to 53 percent of nonfatal falls. Alcohol may increase the likelihood of a fall as much as sixty times in those well over the legal limit for intoxication, compared with those having no alcohol exposure.

Fires and burns are the fourth-leading cause of accidental death in the United States. Studies show that alcohol is involved in as many as half of these deaths. Alcohol exposure is most frequent among victims of fires caused by cigarettes (Book Rags, 2008).

One study of injury morbidity, based on emergency room visits to a Massachusetts general hospital from October 1966 to September 1967, identified alcohol-positive breathalyzer readings of 0.01 percent and higher among 22 percent of 620 persons treated for injuries in the home (Wechsler et al., 1969). And reflecting an area often overlooked in these discussions, the study also noted that positive readings were associated with 56 percent of 188 persons reporting because of injuries from fights and assaults. Positive readings were found for 9 percent of a comparison group admitted for non-injuries.

Research from the United Kingdom may be more helpful in determining the extent of impact. According to the Institute for Alcohol Studies (IAS), there are approximately 4,000 deaths from home accidents annually. Approximately 2.6 million home accidents each year result in the victim visiting an emergency room for treatment. There are similar numbers of cases in which the victim is treated by a general practitioner. In addition, there are millions of minor cases in which no medical assistance is sought.

The IAS report noted that a 2002 UK study found that being under the influence of alcohol emerged as the single most important form of contributory behavior in regard to fatalities and a major factor in regard to serious injuries. Based on this study, the IAS estimated that alcohol is a causal factor in around 10 percent of fatalities from home accidents (Institute of Alcohol Studies, 2007).

A 1998 UK study of accidents, which considered statistics in various countries in the West, noted that the most common form of alcohol-related accident in 1998 was a fall, either on stairs or on the same level. Falls accounted for 41 percent of all alcohol-related home accidents. The next most common form of alcohol-related accident was striking a stationary object (11% of alcohol-related home accidents). The most common type of injury from alcohol-related home accidents in 1998 was an open wound (30%) followed by injury to soft tissue (19%) and bone injuries (13%). Sixty-two percent of alcohol-related accidents in the home involved men and 38 percent involved women (Institute of Alcohol Studies, 2007).

BOATING ACCIDENTS

More than 80 percent of the people who die in boating accidents are drowning victims (State of California, 2003). Because alcohol reduces coordination and balance, the chances of falling overboard as well as drowning are increased in those who have been drinking. In addition, depth perception, reaction time, and night vision are all affected by drinking and increase the chances of accidents on the water. A summary of selected reports indicates the following:

- A 2006 Coast Guard report stated that while alcohol use was a contributing factor in 7 percent of boating accidents, it accounted for nearly twenty percent of all reported fatalities and was the leading cause of boating fatalities (U. S. Coast Guard, 2006).
- According to the Florida Fish and Wildlife Conservation Commission and the Oregon State Marine Board (2008), alcohol contributes to about one-third of all fatal boating accidents.

- About half of all boating accidents involve drugs or alcohol (Boat U. S. Foundation, 2008).
- A study of water traffic accidents in Finland between 1969 and 1995 concluded that alcohol intoxication was a contributing cause of death in 63.0 percent of the fatalities (Lunetta et al., 1998).

THE WORKPLACE

According to the U.S. National Institute for Occupational Safety and Health (NIOSH), 5,734 workers died in 2005 from an occupational injury and more than four million workers had a nonfatal injury or illness. As NIOSH reported:

> Private-sector workers, daily, experience 11,500 nonfatal work-related injuries/illnesses; more than half of these injuries/illnesses require job transfer, work restrictions, or time away from their jobs as a result. Among all workers, not just the private sector, 9,000 workers are treated in emergency departments each day, and approximately 200 of these workers are hospitalized. In 2004, this resulted in an estimated 3.4 million nonfatal injuries and illnesses among civilian workers that were serious enough to be treated in hospital emergency departments.

While there is no one comprehensive study as of 2008 on the impact of drugs, including alcohol, on workplace accidents and injuries, the following information provides a general landscape from which to draw conclusions.

- A two-year study of railroad occupational accident investigations and analysis of post-accident tests showed that approximately one-third of the accidents were associated with positive drug test results, and alcohol and/or drug use was determined to be casually related to the accident (Gust et al., 1990).
- Up to 40 percent of industrial fatalities and 47 percent of industrial injuries can be linked to alcohol use and alcoholism (Bernstein & Mahoney, 1989).
- Employees who use drugs are 3.6 times more likely to be involved in a workplace accident and five times more likely to file a workers' compensation claim (U. S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, 2000).
- The risk of job-related injury associated with substance use increases by 50 percent to 100 percent depending upon the substance used and the frequency and amount of use. (See Zwerling, Ryan, & Orav, 1990; Hingson, Lederman, & Walsh, 1985; Gutierrez-Fisac, Regidor, & Ronda, 1992; Pollock et al., 1998; Moll van Charante & Mulder, 1990; Lewis & Cooper, 1989).
- According to the National Federation of Independent Businesses, one in six workplace deaths and one in four workplace injuries involve drugs or alcohol use (Gaudio, 2006).

There is strong, continuing evidence that drug and alcohol use has a significant causal impact on accidents and injuries.

See also **Accidents and Injuries from Alcohol; Alcohol: History of Drinking in the United States; Dover's Powder; Driving, Alcohol, and Drugs; Fetus, Effects of Drugs on the; Social Costs of Alcohol and Drug Abuse.**

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ACETYLCHOLINE. Acetylcholine (ACh) is a major neurotransmitter in the central and peripheral nervous systems. It is the ester of acetate and choline, formed by the enzyme choline acetyltransferase, from choline and acetyl-CoA. This was the first substance (c. 1906) to meet the criteria of identification for a neurotransmitter. Later, acetylcholine was shown to be the general neurotransmitter for the neuromuscular junctions. In all vertebrate species, it is the major neurotransmitter for all autonomic ganglia and the neurotransmitter between parasympathetic ganglia and their target cells. Acetylcholine neurotransmission occurs widely within the central nervous system. Collections of neurons arising within the brain—the medulla, the pons, or the anterior diencephalon—innervate a wide set of cortical and subcortical targets; some of these circuits are destroyed in Alzheimer's disease.

See also **Neurotransmission; Neurotransmitters; Scopolamine and Atropine.**

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FLOYD BLOOM

ADDICTED BABIES. *See* Alcohol- and Drug-Exposed Infants.

ADDICTION: CONCEPTS AND DEFINITIONS.

This entry deals with concepts related to the basic nature of addiction that are widely used but often misused, and that have undergone significant changes since the term *addiction* first came into the common vocabulary. In the following discussion, the terms are grouped according to themes, rather than being arranged in alphabetic order.

ABUSE AND MISUSE

In everyday English, *abuse* carries the connotations of improper, perverse, or corrupt use or practice, as in child abuse or abuse of power. As applied to drugs, however, the term is difficult to define and carries different meanings in different contexts. In relation to therapeutic agents, such as benzodiazepines or morphine, the term *drug abuse* is applied to their use for other than medical purposes or in unnecessarily large quantities. With reference to licit but non-therapeutic substances such as alcohol, it is understood to mean a level of use that is hazardous or damaging, either to the user or to others, or both. When applied to illicit substances that have no recognized medical applications, such as phencyclidine (PCP) or mescaline, any use is generally regarded as abuse. The term *misuse* refers more narrowly to the use of a therapeutic drug in any way other than what is regarded as good medical practice.

Substance abuse means essentially the same as drug abuse, except that the term *substance* (shortened form of *psychoactive substance*) avoids any misunderstanding about the meaning of drug. Many people regard as drugs only those compounds that are, or could be, used for the treatment of disease, whereas *substances* also includes materials such as organic solvents, salvinorins (magic mint), or toad venoms, that have no medical applications at present but are abused in one or more of the senses defined above.

The best general definition of *drug abuse* is the use of any drug in a manner that deviates from the approved medical or social patterns within a given culture at a given time. This is probably the concept underlying the official acceptance of the term *abuse* in such instances as the names of the National Institute on Drug Abuse (USA) and the Canadian Centre on Substance Abuse. Such official acceptance, however, does not prevent the occurrence of ambiguities such as those mentioned in the next section.

RECREATIONAL OR CASUAL DRUG USE

The two terms, *recreational* and *casual,* are generally understood to refer to drug use that is small in amount, infrequent, and without adverse consequences, but these characteristics are not in fact necessary parts of the definitions. In the terminology recommended by the World Health Organization (WHO), the two terms are synonymous as of 2008. However, *recreational use* really refers only to the motive for use, which is to obtain effects that the user regards as pleasurable or rewarding in some way, even if that use also carries some potential risks. *Casual use* refers to occasional as opposed to regular use and, therefore, implies that the user is not dependent or addicted, but it carries no necessary implications with respect to motive for use or the amount used on any occasion. Thus, a casual user might become intoxicated or suffer an acute adverse effect on occasions, even if these are infrequent.

Occasional use may also be circumstantial or utilitarian, if employed to achieve some specific short-term benefit under special circumstances. The use of amphetamines to increase endurance and postpone fatigue by students studying for examinations, truck drivers on long hauls, athletes competing in endurance events, or military personnel on long missions, are all instances of such utilitarian use. Many observers also consider the first three of these to be abuse or misuse, but some would not regard the fourth example as abuse because it is or was prescribed by military authorities under unusual circumstances, for necessary combat goals. Nevertheless, in all four instances the same drug effect is sought for

the same purpose (i.e., to increase endurance). This example illustrates the complexities and ambiguities of definitions in the field of drug use.

INTOXICATION

Intoxication is the state of functional impairment resulting from the actions of a drug. It may be acute (i.e., caused by consumption of a high dose of drug on one occasion); it may be chronic (i.e., caused by repeated use of large enough doses to maintain an excessive drug concentration in the body over a long time). The characteristic pattern of intoxication varies from one drug to another, depending upon the mechanisms of action of the different substances. For example, intoxication by alcohol or barbiturates typically includes disturbances of neuromuscular coordination, speech, sensory functions, memory, reaction time, reflexes, judgment of speeds and distances, and appropriate control of emotional expression and behavior. In contrast, intoxication by amphetamine or cocaine usually includes raised blood pressure and heart rate, elevation of body temperature, intense hyperactivity, mental disturbances such as hallucinations and paranoid delusions, and sometimes convulsions. The term may be considered equivalent to *overdosage*, in that the signs of intoxication usually arise at higher doses than the pleasurable subjective effects for which the drug is usually taken.

HABIT AND HABITUATION

In everyday English, a *habit* is a customary behavior, especially one that has become largely automatic or unconscious as a result of frequent repetition of the same act. In itself, the word is simply descriptive, carrying no fixed connotation of good or bad. As applied to drug use, however, it is somewhat more judgmental. It refers to regular persistent use of a drug, in amounts that may create some risk for the user, and over which the user does not have complete voluntary control. Indeed, an *alcohol habit* has been defined in terms very similar to those used to define dependence. In older writings, *habit strength* was used to characterize the degree of an individual's habitual drug use, in terms of the average amount of the drug taken daily. Reference to a drug habit implies that the drug use is the object of some concern on the part of the user or of the observer but that it may not yet be sufficiently strongly established to make treatment clearly necessary.

Habituation refers either to the process of acquiring a drug habit or to the state of the habitual user. Since habitual users frequently show increased tolerance (decreased sensitivity to the effects of the drug), habituation is also used in the earlier literature to mean an acquired increase in tolerance. In its early reports, the World Health Organization Expert Committee on Drug Dependence (as it is known as of 2008, after several changes of name) used the term *habituation* to refer to a state arising from repeated drug use, that was less serious than addiction in the sense that it included only psychological and not physical dependence, and that harm, if it occurred, was only to the user and not to others. Drugs were classified according to whether they caused habituation or addiction. These distinctions were later recognized to be based on misconception, because (1) psychological (or psychic) dependence is even more important than physical dependence with respect to the genesis of addiction; (2) any drug that can damage the user is also capable of causing harm to others and to society at large; and (3) the same drug can cause effects that might be classed as *habituation* in one user and *addiction* in another. The WHO Expert Committee later recommended that both terms be dropped from use and that *dependence* be used instead.

PROBLEM DRINKING

In an effort to avoid semantic arguments and value judgments about abuse or addiction, clinical and epidemiological researchers have increasingly made use of objective operational definitions and measures. *Problem drinking* is alcohol consumption at an average daily level that causes problems, regardless of whether these are of medical, legal, interpersonal, economic, or other nature, to the drinker or to others. The actual level, in milliliters of absolute alcohol per day, obviously varies with the individual, the type of problem, and the circumstances. The advantage of this term is that a drinker who may not meet the criteria of dependence or who is reluctant to accept a diagnostic label of alcoholism or addiction can often be led to acknowledge that a problem exists and requires intervention.

ADDICTION AND DEPENDENCE

The term *addiction* was used in everyday and legal English long before its application to drug problems. In the sixteenth century, it was used to

designate the state of being legally bound or given over (e.g., bondage of a servant to a master) or, figuratively, of being habitually given over to some practice or habit; in both senses, it implied a loss of liberty of action. At the beginning of the twentieth century, it came to be used more specifically for the state of being given over to the habitual excessive use of a drug, and the person who was given over to such drug use was described as an addict. By extension from the original meanings of addiction, *drug addiction* meant a practice of drug use that the user could not voluntarily cease, and loss of control over drinking was considered an essential feature of alcohol addiction. The emphasis was placed upon the degree to which the drug use dominated the person's life, in such forms as constant preoccupation with obtaining and using the drug and inability to discontinue its use even when harmful effects made it necessary or strongly advisable to do so.

During the first half of the twentieth century, however, the pharmacological and social consequences of such use came increasingly to be the defining criteria. In 1957, the WHO Expert Committee defined addiction as,

> a state of periodic or chronic intoxication produced by the repeated consumption of a drug (natural or synthetic). Its characteristics include (1) an overpowering need (compulsion) to continue taking the drug and to obtain it by any means; (2) a tendency to increase the dose [later said to reflect tolerance] (3) a psychic (psychological) and generally a physical dependence on the effects of the drug; and (4) detrimental effect on the individual and on society.

Physical dependence is an altered physiological state arising from the regular heavy use of a drug, such that the body cannot function normally unless the drug is present. This state is recognizable only by the physical and mental disturbances that occur when drug use is abruptly discontinued or withdrawn, and the constellation of these disturbances is known as a *withdrawal syndrome*. The specific pattern of the withdrawal syndrome varies according to the type of drug that has been used and usually consists of changes opposite in direction to those originally produced by the action of the drug. For example, if opiate drugs cause constipation, their withdrawal typically produces diarrhea; if cocaine causes prolonged wakefulness and euphoria, the withdrawal syndrome will include profound sleepiness and depression; if alcohol decreases the reactivity of nerve cells, the withdrawal syndrome will include signs of over-reactivity, such as exaggerated reflexes or convulsions. In all cases, however, the withdrawal syndrome is quickly abolished by resumption of administration of the drug or of a substitute drug with a very similar pattern of actions.

It has long been recognized that a person can become physically dependent on a drug given in high doses for medical reasons (e.g., morphine given repeatedly for relief of chronic pain) and yet not show any subsequent tendency to seek and use the drug for non-medical purposes. The WHO Expert Committee revised its definitions and concepts to reflect this knowledge in 1973, substituting the single term *dependence* for the two terms *addiction* and *habituation*. Unfortunately, this change has not yet led to uniform terminology or concepts.

In essence, *dependence* is a state in which the individual cannot function normally—physically, mentally, or socially—in the absence of the drug. A simple definition given in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* published in 1994 by the American Psychiatric Association (*DSM-IV*) includes only one fundamental element: "compulsive use of the drug despite the occurrence of adverse consequences." However, a more detailed description of the *dependence syndrome* includes both physical components (increased tolerance to the drug; repeated experience of withdrawal symptoms; use of the drug to prevent or relieve withdrawal symptoms) and behavioral signs of loss of control over drug use (e.g., increasing prominence of drug-seeking behavior, even at the cost of disruption of other important parts of the user's daily life; use of larger amounts than intended; inability to cut down the amount used, despite persistent desire to do so; and awareness by the user of frequent craving).

Psychic dependence or *psychological dependence* refers to those components of the dependence syndrome other than tolerance and withdrawal symptoms, in particular the urgency of drug-seeking behavior, craving, inability to function in daily life without repeated use of the drug, and the inability to maintain prolonged abstinence. It has been

attributed to a distress or tension, especially during periods of abstinence from the drug, which the user seeks to relieve by taking the drug again. This is, however, really a description, rather than an explanation.

Because of these differences in definition of dependence by different authorities, the term has proven to be less clear than intended and has not displaced the term *addiction* from common use. The latter carries a clearer emphasis on the behavior of the individual, rather than the consequences of that behavior, as in the concept of nicotine addiction. A committee report of the Academy of Sciences of the Royal Society of Canada (1989) concluded that the only elements common to all definitions of addiction are a strongly established pattern of repeated self-administration of a drug in doses that reliably produce reinforcing psychoactive effects and great difficulty in achieving voluntary long-term cessation of such use, even when the user is strongly motivated to stop. It has been suggested by some highly experienced researchers in the field of substance use problems that the next edition of the *DSM* (*DSM-V*) and of the WHO *International Classification of Diseases* (*ICD-11*) should revert to the use of *addiction* in place of *dependence*, because the latter term is more likely to confuse physicians and deter them from giving adequate doses of analgesics to patients with terminal cancer, for example. Others have argued equally strongly against abandoning the term *dependence*, in part because *addiction* carries with it a stigma that discourages patients from seeking treatment, and the question is not yet entirely resolved.

Some studies of the *DSM-IV* criteria for dependence have shown them to be highly reliable and reproducible for nicotine and opioids, good for alcohol and cocaine, and only fair for cannabis, sedatives, and psychostimulant drugs. Some authors have questioned whether separate substance-specific diagnostic criteria for dependence are required, whereas others have argued that despite the differences in reliability for different drugs, overall the patterns of dependence on different substances are more similar than different and that a single set of criteria should be retained. However, several investigators have argued for the inclusion of additional criteria related to severity, such as the number of dependence criteria present in a given case or the frequency of consuming more than five standard drinks of alcohol on a given drinking occasion or comparable measures for other substances. An additional topic of debate is whether behaviors not related to drug use, such as compulsive gambling or compulsive eating, should be regarded as addictions. It is generally accepted that there are many close resemblances between these behaviors and those seen in drug dependence and that the same reinforcement system is involved, but as of the first decade of the twenty-first century, there was not complete agreement that the processes are entirely analogous.

Genetic Factors in Dependence. It has been known for many years that family members of alcohol-dependent patients have a significantly greater risk of becoming dependent themselves than members of the general population do. Although the family environment plays an important role in this greater risk, there is abundant evidence that hereditary factors are also important contributors. Exploration of the genetic mechanisms is an important part of research in the early twenty-first century, not only on alcoholism but on other types of drug dependence as well. A few general principles derived from this research can be stated here.

First, there is not one single gene that determines the risk of dependence; rather, there are a very large number of genes, each encoding one component of the total picture. For example, there are different genes that determine the initial sensitivity to the actions of a drug on first exposure to it, the degree of reinforcement produced by a given dose of a drug, the ability to develop sensitization of the reinforcing effects, the intensity of withdrawal effects if the drug is stopped, the ability to develop tolerance to various effects of the drugs, and so forth. There are also genes that determine the degree of unpleasant or punishing effects of a drug, which may constitute a genetic protection factor against using enough of it to cause problems. Structural variations have been found in many of these genes that can cause both quantitative and qualitative differences in the various drug effects in different individuals and populations.

A second principle is that the degree to which a gene is expressed, that is, the degree to which its action is allowed to proceed or is held in check, can

be affected by non-genetic influences either within the individual's metabolism or in the environment. Therefore, a person who has a gene variant that would increase the risk of some aspect of dependence if it is expressed, but who is not exposed to the environmental risk factor, does not necessarily show such a change and, therefore, does not necessarily become dependent.

A third principle is that even if the person carrying such genetic risk factors does become dependent, the consequences can be strongly affected by environmental influences. For example, both dependent and non-dependent persons use less of a drug if the price is increased or the availability is otherwise decreased. This correlation has been shown not only with alcohol, but also with tobacco, heroin, cocaine, cannabis, and other drugs. Therefore, the impact of dependence on the user, and to a considerable extent on those in contact with the user, can be influenced by social interventions that do not directly treat the dependence itself. This fact has given rise to the philosophy of harm reduction, according to which society can take a variety of measures to decrease the overall harm resulting from drug dependence even if it is not possible to prevent or cure the dependence in many cases.

Subtypes of Dependence. Despite the validity of the general diagnostic criteria, it has been recognized for many years that dependence varies greatly from patient to patient, with respect to the relative prominence of the various features of the clinical picture. This variability has perhaps been examined most in relation to alcohol dependence, where it gave rise many years ago to the concept that there are different subtypes of alcoholism. Later class analyses of large numbers of respondents in epidemiological studies have provided some evidence for the existence of several clusters of patients differing, for example, in frequency of binge drinking, family history, concurrent psychiatric disorders (comorbidity), and use of other drugs. Some attempts have been made to correlate different patterns of gene variations with these different clinical pictures. However, no consistent patterns have been found in different studies as of 2008, and the concept of subtypes has not found wide acceptance, nor has it had significant impact on diagnostic or therapeutic practices.

REINFORCEMENT AND ITS RELATION TO DEPENDENCE

No drug can give rise to dependence unless (1) it produces some effect that causes the user to make efforts to obtain and use the drug again and (2) it is taken frequently enough to establish a strong pattern of drug-related behavior that is resistant to eradication. The effect that leads to repetition of drug-taking is a psychoactive effect, that is to say, an effect that alters the user's perceptions, thoughts, and emotions in a manner that is usually (but not always) experienced as pleasurable or rewarding. The various drugs that are potentially abused or addictive are all thought to act in different ways to stimulate a set of nerve-cell pathways referred to in scientific shorthand as the *reward system*. Activation of this system leads to an increased probability that the behavior that caused the activation (in this case, the drug-taking) will be repeated or reinforced, and the drug is called a *reinforcer*. A drug must have a reinforcing effect if it is to become addictive, but it is important to recognize that reinforcement is not the same as addiction. Reinforcement is an essential mechanism for survival, learning, and adaptation. The satisfaction of thirst by drinking water, of hunger by eating food, and the avoidance of harm by escape are all examples of types of reinforcement by natural and necessary behaviors. Addictive drugs are regarded as *usurpers* of the reward system that produce reinforcement by direct drug action on it without serving any necessary biological function.

Nevertheless, drug-induced reinforcement, like reinforcement by food, water, sexual activity, or escape from harm, simply means that the behavior that caused it has an increased likelihood of being repeated. Some other process or processes must enter into play if that behavior is to become so strongly entrenched that it comes to dominate the individual's thinking and activities. Various hypotheses have been put forward concerning the nature of such additional processes. One suggestion is that activation of the reward system is controlled by something analogous to a thermostat regulating the set-point of the system, and that frequent repetition of drug-taking leads to a change in set-point so that reinforcement grows progressively stronger over time. Another, perhaps related, hypothesis is that the degree of reinforcement by a given drug is regulated by genetic factors; therefore, vulnerability

to addiction is greater in those who inherit either an abnormally high sensitivity to the reward system or a low sensitivity to the aversive (punishing, disagreeable) effects of the drug. Another view holds that the essential feature leading to addiction is not reward (i.e., pleasure or liking for the drug) but drug-induced sensitization of the process of incentive saliency (i.e., the subjects' awareness of, and wanting for, drug-related stimuli becomes progressively greater, so that they have a steadily increased probability of controlling behavior). Yet another, and closely related, hypothesis is that drug-taking generally occurs within certain specific environmental or social contexts, and cues arising from these contexts can become linked to the drug effects as conditional stimuli, which then become able to elicit drug-taking behavior and further reinforcement. This concept of the conditioned stimulus is analogous to the role of the bell in Pavlov's experiments in which salivation, at first elicited by the feeding of meat to a dog, could eventually be elicited by the bell alone if the bell was always sounded just before the presentation of the meat. In this view, when the drug-taking comes under the control of such extraneous stimuli and is no longer a purely voluntary act, the transition to addiction has occurred. These various hypotheses, and possibly others, require much further research before the relation of reinforcement to addiction can be fully explained. Moreover, all such hypotheses must recognize that the degree of risk that any given individual will become addicted to a particular drug, even a strongly reinforcing one such as cocaine, is strongly influenced by environmental, social, economic, and other factors.

Neurobiological Elements of the Reward System. The first link in the set of nerve cell pathways constituting the reward system is a group of cells in the midbrain (ventral tegmental area or VTA) that give rise to fibers running to cells in the base of the forebrain (Nucleus accumbens or NAc) and in the prefrontal cortex (PFC), where they release the transmitter chemical dopamine. This chemical stimulates cells in both the NAc and the PFC, and fibers from these cells in turn release chemical transmitters that act upon other cells in various parts of the brain. Many of them send fibers back to the VTA, where they release glutamate, which increases the activity of the dopamine cells; in contrast, cells in the NAc send fibers back to the VTA that release gamma-aminobutyric acid (GABA), which decreases the activity of the dopamine cells. In addition, the activity of the VTA dopamine-releasing cells and of the NAc cells is normally influenced by a variety of chemicals (including histamine, serotonin, orexin, morphine-like peptides, cannabis-like fatty materials, corticotropin releasing factor, and others) formed in and released from other nerve cells, some of which stimulate cell activity whereas others inhibit it. Thus, the level of activity of the dopamine cells, and hence of the other cell types that they act upon, is controlled by the changing balance among a variety of influences that adjust it in response to changes within the body and in the surrounding environment.

Different addictive drugs affect the dopamine cells in the VTA by different mechanisms. For example, cocaine and amphetamine directly stimulate the release of dopamine from the endings of the nerve fibers in the NAc and the PFC, or inhibit the reuptake of dopamine into the nerve endings; morphine-like drugs inhibit the release of GABA and thus free the dopamine cells from GABA inhibition, so that they become more active. Orexin from the hypothalamus and cannabis-like fatty materials (endocannabinoids) act directly on target sites (receptors) on the VTA cell bodies, the former to stimulate the dopamine cells and the latter to inhibit them.

It was formerly thought that the release of dopamine from the endings of the VTA cell fibers onto cells in the NAc directly resulted in reinforcement, but there is as of 2008 much evidence that its effect is to alert other parts of the brain to a novel stimulus, such as a drug effect, that may or may not be rewarding. The effects of the released dopamine on the activity of the cells in the NAc, the PFC, and other sites in the brain, as well as the actions of the drugs directly at those other sites, are presumably responsible for producing the rewarding or reinforcing effects.

The research in the 2000s on neurobiological factors in reinforcement and in addiction has provided some rational basis for the identification and testing of potential therapeutic agents for the treatment of dependence. For example, endogenous opioid peptides (e.g., endorphins, enkephalins) act through inhibitory receptors found on GABA-releasing nerve endings that affect both VTA dopamine neurons and

their fiber endings that activate cells in the NAc; by inhibiting the release of GABA, they allow the VTA and NAc cells to become more active. Therefore, an opioid receptor blocker such as naltrexone, which prevents the action of opioid peptides as well as that of heroin or morphine, will also block the first steps of the reinforcement or reward process, regardless of which drug is initiating the VTA cell activation. Thus, naltrexone has been found to be moderately useful in treating patients with alcohol dependence, as well as those with heroin dependence. Similar basic neurobiological discoveries have given rise to therapeutic trials with acamprosate in alcohol dependence, with serotonin 5-HT3 receptor blockers such as ondansetron in nicotine and alcohol dependence, and with activators of GABA receptors such as baclofen and topiramate in alcoholism and in cocaine dependence.

Progression from Drug Use to Dependence. Reinforcement can occur as a result of the first exposure to a drug, yet the great majority of occasional users, even of drugs such as cocaine or heroin, do not become dependent or addicted. Therefore, some additional change must occur as a result of repeated drug exposure in those users who do become dependent. Many neurobiologists believe that the additional change is a process known as synaptic plasticity, that is, adaptive changes in synapses (functional cell-to-cell contact sites) on cells such as those in the VTA and NAc that render them more easily stimulated and increase their output of neurotransmitter substances. According to this view, the result of such changes would be that the reinforcing effect of the drug is increased and, therefore, comes to control the person's behavior and direct it increasingly toward drug-seeking and drug use. An alternative concept is that the balance of the various stimulatory and inhibitory influences on the activity of the dopamine cells in the VTA is regulated by something analogous to a thermostat and that with repeated use of a drug, the set point is shifted in such a manner that the user gets less reward from the usual dose and is thus motivated to increase the amount used. Among young adult users of alcohol, for example, those who experience relatively little effect from an ordinary sized drink are much more likely to have become dependent five years later.

These concepts imply that the actions of the drugs themselves initiate adaptive changes that convert drug use into dependence. Yet epidemiological studies have found that as many as 34 percent of patients with a diagnosis of dependence according to *DSM-IV* criteria did not have a preceding history of abuse (usually implying bouts or binges of heavy use), and patients with a diagnosis of abuse do not always progress to dependence. These findings suggest that production of dependence may require some additional causal factor that is independent of those factors giving rise to abuse. The additional causal factor could be a separate genetic risk factor, or some influence in the person's physical or psychological environment. This question clearly requires considerably more research.

RELAPSE AND REINSTATEMENT

As noted earlier, addiction or dependence is not characterized by an inability to stop using the drug, but by an inability to maintain the cessation of use. A high proportion of dependent patients do make efforts to stop drug use and, in fact, do stop for varying periods of time, but then they resume drug use even though they would wish not to do so. This pattern of behavior is known clinically as relapse, and patients may have many short periods of abstinence followed by relapse. Much research into the causes of relapse has been carried out in both clinical and laboratory settings. In humans, relapse most commonly occurs either when the social setting provides an opportunity to take a small amount of the drug, or when the patient experiences sudden emotional or physical stress.

Animal research has made increasing use of a model in which the animal is taught to press a lever in order to obtain a small dose of a drug (e.g., morphine, alcohol, cocaine) when a signal light informs it that the drug is available. Most (but not all) of these animals will then steadily increase their total intake per session when given the opportunity to do so, until they take the drug in preference to food or water, and will develop a drug withdrawal syndrome if the drug is suddenly stopped. These animals are regarded as a model of dependent humans. They are then subjected to a procedure known as extinction, in which they are allowed to press the lever in response to the drug-availability signal, but the drug is not delivered.

After a varying number of such trials, they learn that the lever-pressing response to the signal is not rewarded, and they stop pressing the lever. This is regarded as an animal model of treatment-related abstinence in the human. If the animal is then given a small intravenous dose of the drug, or a stressful stimulus such as a small electric shock to the feet, it will rapidly resume pressing on the drug lever in response to the drug-availability signal, even if the drug is still not made available as a result. This is regarded as an animal model of relapse in humans. However, since it is impossible to know whether the animal is experiencing the same types of internal disturbance as the human patient does in relapse, the operational term *reinstatement of drug-seeking behavior* is generally used in place of *relapse*. This animal model can then be used to test the ability of various drugs or procedures to prevent reinstatement, so that effective ones can be explored for possible therapeutic use to prevent relapse in humans.

CRAVING AND RELATED CONCEPTS

Craving refers to an intense desire for the drug, expressed as constant, obsessive thinking about the drug and its desired effects, a sense of acute deprivation that can be relieved only by taking the drug, and an urgent need to obtain it. This state is probably induced by exposure to bodily sensations and external stimuli that have become conditional stimuli by being linked in the past to circumstances and situations in which drug use has been necessary, such as self-treatment of early withdrawal symptoms by taking more drug. If those sensations or external stimuli are then produced by other means, they can give rise to the same mental states and behaviors as those that had formerly been brought about by drug withdrawal, including craving, and thus can cause a relapse. *Drug hunger* is essentially synonymous with craving, and *urge* represents the same phenomenon but of lesser intensity.

The behavioral consequence of an urge or craving is usually a redirecting of the person's thoughts and activities toward obtaining and using a new supply of drug. All the behaviors directed toward this end, such as searching drawers and cupboards for possible remnants of drug, getting money (whether by legal or illegal means), contacting the sources of supply, purchasing the drug, and preparing it for use, are included under the term *drug-seeking behavior*. The more intense the craving, the more urgent, desperate, or irrational this behavior tends to become.

TOLERANCE AND SENSITIZATION

The term *tolerance*, which has long held a prominent place in the literature on drug dependence, has a number of different meanings. All of them relate to the degree of sensitivity or susceptibility of an individual to the effects of a drug. *Initial tolerance* refers to the degree of sensitivity or resistance displayed on the first exposure to the drug; it is expressed in terms of the degree of effect (as measured on some specified test) produced by a given dose of the drug or by a given concentration of drug in the body tissues or fluids: The smaller the effect produced by that dose or concentration, the greater is the tolerance. Initial tolerance can vary markedly from one individual to another or from one species to another, as a result of genetic differences, constitutional factors, or environmental circumstances.

The more frequent meaning of *tolerance*, however, is *acquired tolerance* (or acquired increase in tolerance), that is, increased resistance or decreased sensitivity to the drug as a result of adaptive changes produced in the body by previous exposure to that drug. This factor is expressed in terms of the degree of reduction in the magnitude of effect produced by the same dose or concentration, or (preferably) the increase in dose or concentration required to produce the same magnitude of effect. Acquired tolerance can be due to two quite different processes. *Metabolic tolerance* (also known as *pharmacokinetic tolerance* or *dispositional tolerance*) is produced by an adaptive increase in the rate at which the drug is inactivated by metabolism in the liver and other tissues. This response results in lower concentrations of drug in the body after the same dose, so that the effect is less intense and of shorter duration. *Functional tolerance* (also known as *pharmacodynamic tolerance* or *tissue tolerance*) is produced by a decrease in the sensitivity of the tissues on which the drug acts, primarily the central nervous system, so that the same concentration of drug produces less effect than it did originally.

Acquired functional tolerance can occur in three different time frames. *Acute tolerance* is that

which is displayed during the course of a single drug exposure, even the first time it is taken. As soon as the brain is exposed to the drug, compensatory changes begin to develop and become more marked as time passes. As a result, the degree of effect produced by the same concentration of drug is smaller in the later part of the exposure than it was in the early part; this phenomenon is sometimes called the *Mellanby effect.* A second time pattern of tolerance development is known in the experimental literature as *rapid tolerance.* This term refers to an increased tolerance seen on the second exposure to the drug, if this occurs not more than one or two days after the first exposure. *Chronic tolerance* is that form of acquired tolerance that develops progressively over an extended period of time in which repeated exposure to the drug takes place. There is suggestive evidence that these three forms may involve the same or very similar mechanisms. As of 2008, all experimental interventions tested produced virtually identical effects on rapid and chronic tolerance, and chronic tolerance is accompanied by an increase in the rate of development of acute tolerance.

Although acquired tolerance involves important physiological changes in the nervous system, it is also markedly influenced by learning. Tolerance develops much more rapidly if the individual is required to perform tasks under the influence of the drug than if the same dose of the same drug is experienced without any performance requirement. Similarly, environmental stimuli that regularly accompany drug administration can come to serve as Pavlovian conditional stimuli that elicit tolerance as a conditional response, so that tolerance is demonstrated much more rapidly in the presence of these stimuli than in their absence.

Sensitization refers to a change opposite to tolerance that occurs with respect to certain effects of a few drugs (most notably, central stimulant drugs such as cocaine and amphetamine, or low doses of alcohol that produce behavioral stimulation rather than sedation) when these are given repeatedly. The degree of effect produced by the same dose or concentration grows larger rather than smaller. For example, after repeated administration of amphetamine, a dose that initially produced only a slight increase in physical activity can come to elicit very marked hyperactivity, and a convulsion can be produced by a dose that did not initially do so. This fact does not apply to all effects of the drug, however; tolerance can occur toward some effects (such as the inhibition of appetite) at the same time that sensitization develops to others. The reason for this difference was not yet known in the early twenty-first century.

CROSS-TOLERANCE AND CROSS-DEPENDENCE

The term *acquired tolerance* is applied to tolerance developing to the actions of the same drug that has been administered repeatedly. However, if a second drug has actions similar to those of the first, an individual who becomes tolerant to the first drug is usually also tolerant to the second drug, even on the first occasion when the latter is used. This phenomenon is called *cross-tolerance*, and it may be partial or complete: It may extend to all the effects of the second drug or only to some of them. The adaptive changes in the nervous system that give rise to acquired tolerance are believed by most researchers (though not all) to be responsible also for the development of physical dependence. Thus, an adaptive change in cell function, opposite in direction to the effect of the drug, will offset the latter when the drug is present (tolerance) but will give rise to a withdrawal sign or symptom when the drug is removed. The term *neuroadaptive state* has been proposed to designate all the physiological changes underlying the development of tolerance and physical dependence. If the second drug, to which cross-tolerance is present, is given during withdrawal from the first, it can prevent or suppress the withdrawal effect; this response is known as *cross-dependence.* A related concept is that of *transfer of dependence*, from a first drug on which a person has become dependent to a second drug with similar effects that has been given therapeutically to relieve the withdrawal signs produced by the first.

See also **Models of Alcoholism and Drug Abuse.**

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ADDICTION (JOURNAL). *Addiction* is a monthly, peer-reviewed scholarly journal that has been in continuous publication since 1884. Addiction publishes peer-reviewed research reports on alcohol, illicit drugs, tobacco, and gambling. Its research reports cover epidemiology, treatment, prevention, policy, medical consequences, as well as social, psychological, and genetic causes. In addition

to original research, the journal publishes editorials, commentaries, reviews, historical articles, letters, book reviews, and interviews. As an international medium of scientific exchange, the journal has its head office in Great Britain with regional offices in the United States and Australia.

THOMAS BABOR

ADDICTION SEVERITY INDEX (ASI). The Addiction Severity Index (ASI) is a semi-structured interview designed to provide important information about the nature and severity of substance use as well as information about other life problems that may contribute to or result from that substance use. Developed by A. Thomas McLellan and coworkers in 1980, the ASI has been translated into twenty-two languages (Japanese, French, Spanish, German, Dutch, and Russian among them) and was designed to be administered by a technician or counselor. Consistent guidelines for each question on the ASI have been compiled in training materials including two videos and three instructional manuals. Self-training can be accomplished by using the video along with the administration manual, although a one-day formal training seminar is recommended. The instrument is in the public domain, and so there is no charge for it; only a minor fee is charged for copies of the administration materials and the computer scoring disk.

The interview is based on the idea that addiction to drugs or alcohol is best considered in terms of the life events that preceded or resulted from the substance-abuse problem. The ASI focuses on seven functional areas, or subscales, that have been widely shown to be affected by the substance abuse: medical status, employment and support, drug use, alcohol use, legal status, family and social status, and psychiatric status. Each of these areas is examined individually by collecting information regarding the frequency, duration, and severity of symptoms or problems, both historically over the course of the patient's lifetime and more recently during the thirty days prior to the interview. Within each of the problem areas, the most recently published version—ASI-5—provides both a 10-point, interviewer-determined severity rating of lifetime problems as well as a multi-item composite score (computer-calculated) that indicates the severity of problems in the past thirty days.

The ASI-5 contains 164 items in the seven problem areas. It requires approximately 45–75 minutes to administer initially, depending upon the number and nature of the problems presented, and about 20–25 minutes to administer at follow-up because the follow-up version excludes the lifetime items. The most reduced form of the instrument is the ASI-Lite: a shortened form that provides composite scores and historical information but not the interviewer severity ratings nor the grid of questions asking about family/genetic heritability. It contains 111 questions and requires approximately 30–40 minutes to administer initially as a semi-structured interview, and about 15–20 minutes to administer at follow-up to measure change. The ASI has been used in over 300 studies in the United States and the European version (EuropASI) has been used in about 100 more. The updated normative information for U.S. adults in addiction treatment was presented in a study conducted by McLellan and colleagues in 2005.

Despite the wide use and historical reliability and validity of the ASI, by 2005 there had been many changes in the kinds of drugs used and in the kinds of additional problems seen among drug users. Moreover, the instrument had become popular among a wide range of new users and was being used for different agencies and populations including welfare, criminal justice, employment, the homeless, and primary psychiatric populations. In addition there were problems with the instrument, such as significant training requirements for interviewers, very few cost-relevant items, and low reliability for two of the composite scores. Thus the 2005 group completed a thorough revision, under the direction of John Cacciola, published in 2006. The new version—called the ASI-6—is still designed primarily for use with substance-abusing adults who are in substance abuse treatment or research settings, though use with other populations might also be appropriate in certain circumstances. Interviewer severity ratings have been eliminated, and a 6-month time frame has been added to the 30-day frame for cost estimation purposes. While items have been added to update coverage, there

are now branching questions that, if answered negatively, allow the interviewer to skip all subsequent questions related to that topic. This helps to keep administration time at less than one hour. Finally, training is substantially reduced because, as they are written, the items are now designed for administration.

Following more than 25 years of use in the field, there appear to be three reasons for acceptance of the ASI. First, the ASI is able to validly characterize and quantify the severity of the multiple health and social problems found among those with substance use disorders. Knowledge about the nature and severity of these health and social problems is key to developing an appropriate treatment plan for predicting the course of treatment and for fully evaluating treatment interventions. The second reason is that the ASI is free and in the public domain, which accounts for the wide commercial interest in developing software and training products to support its use. Finally, there has been an ongoing effort to refine, validate, and improve the ability of the ASI to measure contemporary issues in addiction treatment. As indicated, availability of the sixth version of the ASI is imminent, and this has been necessary to keep the instrument contemporary with the new discoveries in the addiction field and to correct problems in earlier versions.

See also **Addiction: Concepts and Definitions; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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ADDICTIVE PERSONALITY AND PSYCHOLOGICAL TESTS.

The term *addictive personality* has been used in various ways since the 1940s, usually to refer to a pattern of traits

commonly observed in alcoholics and other substance abusers. The traits include impulsivity, immaturity (dependency and neediness), poor frustration tolerance, anxiety, and depression. Long-term studies of addicts have shown that these characteristics often diminish during abstinence. This suggests that they are produced by the drugs—or by the life that drug use imposes—or are a response to social conditions, rather than caused by inherent personality. However, the term has also been used to describe related personality traits (e.g., early difficulties with impulse control and submission to authority) that may predate drug abuse/dependence and hence serve as predictors of such behaviors. Although addiction researchers have repeatedly correlated several types of personality disorders with alcohol and drug abuse, they have largely rejected the concept of addictive personality, and it is not a recognized diagnostic term in the *Diagnostic and Statistical Manual* (*DSM*) or the *International Classification of Diseases* (*ICD*). Substance use research during the past 50 years has made it clear that the etiology of addictive behaviors is enormously complex, involving an array of physiological, social, demographic, and situational factors in addition to individual personality traits. Psychological approaches to addiction have come to focus more heavily on understanding how addictive behavior is motivated. Motivational models include positive reinforcement (drugs make the user feel good), negative reinforcement (drugs reduce or remove the experience of feeling bad), and the roles played by various other cognitive processes, such as expectations and beliefs. Such models are gradually being clarified by ongoing research in brain science, which elucidates the neuropharmacological processes of behavioral responses to abused substances.

That said, psychological testing—including that focused on personality—has been and remains a key part of the assessment process for alcohol and drug abuse/dependence. Psychological tests and measurements (psychometrics) are structured ways of evaluating an individual's inner mental life and external behaviors. They present subjects with more or less standard stimuli, to which the subjects respond. Depending on the test, these responses reveal something about subjects' intelligence, abilities and skills, educational and vocational interests and achievements, and personality. Often the tests are especially helpful in diagnosing organic brain disease—its presence, its presumed location, and the particular resulting functional deficits. The tests themselves range from structured questionnaires or interviews to written tasks, to obtaining responses to purposely ill-defined stimuli such as ink blots (Rorschach test). They have been used (1) to evaluate the probability of the presence of a substance abuse problem, (2) to examine the impact of substance use on behavior and brain function, both acutely and chronically, and (3) to assess personality features—profiling those predisposed to drug use and abuse or those that are the results of such use.

There are dozens of such testing instruments available to clinicians and researchers. Some of them are broadly applicable, and others are designed for specific populations (e.g., adolescents). Some assess underlying personality traits; others track recent drug use patterns, and yet others reflect long-term chronic use patterns. They vary in their utility in different stages of assessment and treatment (i.e., screening, diagnosis, assessment of substance-using behavior, treatment planning, treatment and process assessment, and outcome evaluation). Psychometric instruments also vary in their reliability (how generalizable the instrument is across different times, settings, scale versions, evaluators, etc.) and their validity (e.g., ability to comprehensively sample the domain of interest, the relation of test scores to subjects' real-world behavior, and the degree to which the test reveals an underlying causal or explanatory dimension of behavior). During the first few decades that they were used to identify possible personality correlates of alcohol and drug abuse, the tests often yielded inconsistent results. Depending on the test, drug-user personality traits could include low self-esteem, sensitivity to disapproval, anxiety, depression, low frustration tolerance, hedonism, helplessness, gregariousness, being a loner, shyness, aggressiveness, impulsiveness, immaturity, and a number of others. Such discrepancies likely stem from differences in the way the groups of substance abusers were defined, the fact that many patients abuse more than one drug, differences in the severity of substance abuse among patients, and the frequency of coexisting psychiatric disorders in many of those tested.

The Minnesota Multiphasic Personality Inventory (MMPI) has been and continues to be the personality test most frequently used to assess substance abusers. Because some MMPI test items that correlate well with

substance abuse also correlate with other disorders, three supplementary scales, the MacAndrew Alcoholism Scale (MAC), the Addiction Admissions Scale (AAS), and the Addiction Potential Scale (APS), were designed specifically to detect substance abuse. Of these, the MAC, developed in 1965, has been the most extensively used and studied. MacAndrew constructed the scale by contrasting MMPI responses of male alcoholics with those of nonalcoholic male psychiatric patients and then selecting the test items that differentiated the two groups. None of the items directly assesses substance abuse behavior; rather, they tap personality factors often associated with such behavior, such as rebelliousness, aggressiveness, risk-taking, and pleasure-seeking. A recent review of studies using the MAC found that the test correlates well with measures of alcohol and substance abuse in adults and adolescents (both male and female) across a diverse spectrum of use and abuse patterns. It works well in differentiating substance abusers from nonabusing nonpatient populations, but it does not discriminate nearly as well between substance abusers and psychiatric patients who are not substance abusers. Some studies have found that individual MAC scores remain fairly consistent even after treatment. Because the MMPI was of limited use in assessing the likelihood of drug abuse, subjective effects questionnaires such as the Addiction Research Center Inventory (ARCI) were developed. The ARCI, developed in the early 1960s at the National Institute of Mental Health, measures a broad range of physical, emotive, cognitive, and subjective effects of drugs. Patients are generally tested before and repeatedly after administration of a single dose of a given drug.

Future addiction research and assessment may well refine the accuracy of psychometric instruments, providing more information about the role of such factors as age, gender, ethnicity, culture, and even genetics in substance abuse problems. Such problems, as one author has noted, remain complex, multidimensional, multidetermined, nonlinear, and dynamic entities that resist attempts to reduce them to personality profiles.

See also **Addiction: Concepts and Definitions; Minnesota Multiphasic Personality Inventory (MMPI).**

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ADOLESCENTS AND DRUG USE.

Adolescence, generally defined as the teenage years, bridges childhood and adulthood. During this period, pubertal development is concluded, the brain undergoes reorganization of functional circuitry, intellectual capacities attain plateau, and physical growth is completed. These biological processes are complemented by the assumption of adult roles (e.g., working), accompanied by expansion of the behavior repertoire concomitant to attaining majority age (e.g., sex, driving a car, substance use).

EPIDEMIOLOGY

A 2007 epidemiological survey indicated that 48.2 percent of high school seniors had tried an illicit drug, 56.4 percent had experienced alcohol intoxication, and 47.1 percent had smoked cigarettes (Johnston et al., 2007). Notably, thirty-day prevalence of tobacco use among high school seniors declined from 19.6 percent in 1975 to 6.2 percent in 2005 in boys and from 16.1 percent to 5.2 percent in girls. Social policies limiting access, increasing the cost of cigarettes through taxation, and social marginalization of users have had significant impact on reducing smoking prevalence. Although adolescents recognize the harmfulness of tobacco, this attitude change has not generalized to consumption of other widely used drugs. Results obtained in the Monitoring the Future Survey in 1975 indicated that occasionally smoking marijuana was perceived as harmful by 18.1 percent

of the twelfth grade population, which rose to 25.9 percent in 2006. Despite the increased perception of harmfulness, 10.2 percent of youths smoked marijuana to get "very high" in 1975 compared to 10.5 percent in 2006. These findings illustrate that there has been no change in the subset of the population that is at highest risk for developing problems consequent to drug use.

Substance use is one facet of initiating adult behaviors. Consumption does not, however, invariably portend long-term problems or addiction. The results of longitudinal research indicate that youths who experiment with drugs may even have better long-term social adjustment than abstainers (Tucker et al., 2006). This finding should not be interpreted to imply that substance use is safe or inconsequential, but rather to underscore the point that exposure does not inevitably presage lasting severe disorder.

ETIOLOGY

Whereas prevalence of substance use disorder consequent to use of illegal drugs is higher in adult males than females (10.3% vs. 6.4%) a much smaller gap is observed in adolescents (5.4% vs. 4.9%) (SAMHSA, 2003). Notably, significant heritability of substance use disorder has been reported in male and female adolescents (Silberg et al., 2003). Moreover, the genetic factors contributing to risk are largely the same across the different classes of illicit drugs in males (Tsuang et al., 1998) and females (Karkowski et al., 2000).

Genetic factors alone cannot cause drug use or addiction. A facilitating environment that affords the opportunity for consumption is a necessary condition. During adolescence, peers exert a critical influence on substance use initiation. Consequently, most youths receive their first drug offer and have their first substance use experience in the context of peer interactions. A pattern of habitual substance use is most likely to develop when the friendship network consists of socially non-normative youths.

Genetic and environmental factors interact to produce biobehavioral phenotypes (observable characteristics) during adolescence that potentiate the risk for drug use initiation, habitual consumption, and subsequent diagnosis of a substance use disorder. The key characteristics promoting this trajectory from initiation to diagnosis of disorder are noted below.

Neurological Maturation. Dramatic neurological changes occurring during adolescence strongly influence the risk for substance abuse. During this period, the brain undergoes reorganization of neural circuitry, especially in the frontal cortex, which subserves regulation of emotion and behavior as well as the higher cognitive capacities integral to strategic thinking, self-monitoring of behavior, and appraisal of future consequences (Spear, 2000). The constellation of high emotion reactivity, behavior undercontrol and limitations in consequential thinking is overtly expressed as a propensity for risk taking and indifferences to societal norms, which, in a facilitating environment (e.g., high drug availability, peer drug use), predisposes to substance use.

Sexual maturation. Precocious onset and rapid progression of puberty are also associated with increased risk of substance abuse (Kirillova et al., 2001). The emergence of secondary sex characteristics (e.g. facial hair in boys, breast development in girls) evokes the appearance of maturity beyond chronological age that may lead to acceptance into an older peer cluster that introduces the youngster to abusable substances. In addition, elevation in testosterone level in adolescent boys is associated with a propensity toward social dominance and low adherence to social norms that, in turn, promotes substance abuse (Reynolds et al., 2007).

Interpersonal Adjustment. Adolescence is a critical period of socialization. Multiple roles and responsibilities of adulthood are increasingly adopted as the youngster transitions from the primarily family sphere of influence to the influences of peers in the workplace, school, and recreation settings. Driving a car provides mobility, and earning money yields resources, to access and purchase abusable substances in these environments. Susceptibility to peer pressure, combined with the desire for acceptance in the popular peer cluster, further amplifies risk for substance use.

Psychological Characteristics. The most prominent psychological characteristic predisposing to substance use is undercontrolled behavior. This is manifest broadly as conduct problems and indifference to societal norms. A temperament disposition in early childhood marked by poor self-regulation (e.g., restlessness, irritability, excitability) in severe cases commonly precedes attention deficit hyperactivity disorder (ADHD) and conduct disorder (CD) by late childhood that, in turn, leads to substance abuse in early adolescence. The same genetic factors largely underlie CD, ADHD, and substance use disorder. Moreover, drug/alcohol exposure during fetal development, and having parents with poor childrearing skills, or low investment in the child, hampers the child's development of self-regulation. The dysregulated adolescent domiciling in a family where there is inadequate supervision is prone to engage in risky behaviors. Specifically, the ubiquity of drugs in the social environment, combined with high offer rates from peers, potentiates substance abuse in psychologically dysregulated youths.

Psychological dysregulation in late adolescence amplifies risk for antisocial personality disorder in boys and borderline personality disorder in girls. These are the most frequent gender-related personality disturbances presaging and co-occurring with substance use disorder. Concomitant to mating assortment, occurring commonly by late adolescence, both members of the couple evincing poor self-regulation are prone to substance abuse and substance use disorder. Conflict and violence in the relationship is exacerbated by the acute disinhibiting effects of drugs. Their children are also at elevated risk for substance use disorder at a young age concomitant to high genetic loading, disrupted family milieu, and parents who have low skill or investment in child rearing.

DEVELOPMENTAL PERSPECTIVE

Substance use among adolescents is a developmental outcome. Consumption may be experimental and thus transitory. Alternatively, it may remain nonproblematic, but habitual behavior throughout life. However, onset of substance use at an early age, especially where there is also disruptive behavior, augments risk for substance use disorder during adolescence.

Recognition of the adverse impact of addiction on physical and mental health and social adjustment has catalyzed research directed at delineating the characteristics of vulnerable youths and the natural history of addiction. One long-standing view of etiology has been framed as the "gateway hypothesis" (Kandel, 2002). In this theory, consumption of legal drugs is conjectured to provide the impetus to use "soft" illegal drugs, specifically marijuana, which in turn predisposes to "hard" drug use. The pharmacological characteristics of the drug earlier in the sequence and associated risk factors related to consumption of the next drug in the sequence are argued to comprise the mechanisms promoting transitions from one type of drug to the next. The notion of a gateway sequence is, however, not substantiated by empirical evidence. Rather, research findings point to common liability (Vanyukov et al., 2003). A trait integral to this liability, termed *neurobehavior disinhibition*, consisting of cognitive competence, behavior control, and emotion modulation predicts substance abuse in adolescents and diagnosis of a substance use disorder by young adulthood (Tarter et al., 2003).

ASSESSMENT

The Drug Use Screening Inventory was developed and subsequently revised (DUSI-R) to quantify the processes that predispose to and correlate with adolescent substance abuse (Tarter & Kirisci, 2001). This 149-item self-report questionnaire evaluates severity of disturbances in ten domains: (1) substance use, (2) behavior problems, (3) health, (4) psychiatric status, (5) school, (6) family, (7) peers, (8) social competence, (9) work, and (10) leisure/recreation. The respondent's profile readily informs about the areas of disturbance that require intervention. Because administration takes only about fifteen minutes, and scoring is automatic using a Web-based format, it is widely used to identify high-risk youths who require prevention intervention as well as to document changes during treatment and aftercare.

PREVENTION

Prevention interventions have yielded only limited long-term benefit primarily because programs

target one or only a few aspects of the risk for substance abuse and have insufficient duration and intensity. Effective prevention needs to target parents who have a substance use disorder so that they can be inculcated with the skills needed to raise a child who is at elevated genetic and environmental risk. Prevention also needs to be directed at women who are pregnant because alcohol and drug consumption during gestation may compromise neurological development in the fetus, which manifests postnatally as disinhibited behavior. This psychological propensity amplifies risk for early age onset substance abuse and substance use disorder. Furthermore, preventions need to be implemented in the early postnatal period to strengthen parent-infant attachment. Bonding is the foundation of parental motivation to supervise the child. Preventing neglectful parenting is especially important as the child transitions into adolescence when the opportunities for substance abuse sharply increase. Notably, providing parental support, such as home visitations by nurses, has a long-term positive impact on the child's outcome (Olds et al., 2003).

Social, educational, and health institutions need to be utilized, therefore, in a coordinated manner to identify and ameliorate the cognitive, emotional, and behavioral characteristics that render the youngster susceptible to initiating substance consumption. Accordingly, effective prevention requires a sustained effort directed at promoting healthy psychological development. Youths having attitudes and a behavior disposition that align with societal norms can be restrained from participating in environments where there is high drug availability (e.g., unsupervised parties, affiliation with socially deviant peers). Hence, a key feature of effective prevention is long-term commitment to the child's welfare such that the ubiquity of drugs in the environment can be managed through effective parenting complemented by inculcation of normative values and behaviors in the child.

See also **Conduct Disorder and Drug Use; Coping and Drug Use; Monitoring the Future.**

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RALPH TARTER

ADULT CHILDREN OF ALCOHOLICS. Individuals over the age of eighteen with at least one biological parent with a history of severe, chronic alcohol problems are labeled "adult children of alcoholics" (ACOA). This label is generally stigmatizing, but studies have shown that this stigmatization may be unwarranted. A 2000 review of the literature by S. L. Harter found that studies have noted greater depression, anxiety, stress-related disorders, maladjustment, and relationship problems in ACOA compared to adult children of nonalcoholics (ACONA). However, Harter also found that many of these studies were based on a clinical or convenience sample, lacked appropriate comparison groups, and had poor measurements.

RISKS INVOLVED WITH ACOA

According to L. Chassin and colleagues (1991), ACOA are predisposed to alcohol and drug problems beginning in adolescence, while children of alcoholics are 5.1 times more likely to report dependence symptoms related to substance use than children of nonalcoholics. Longitudinal cohort studies by J. Knop and colleagues (2007) show that drinking problems continue into adulthood. In addition, compared to ACONA, ACOA may be more likely to choose alcoholic spouses, and they are less likely to reduce their drinking when they enter the workforce, marry, and become parents (Jackson et al., 2001; Flora & Chassin, 2005). However, these problems are not consistently observed in ACOA, and they might apply equally well to dysfunctional families generally.

Alcohol's influence on ACOA is difficult to isolate because alcohol-related familial dysfunction is intertwined with antisocial personality disorder (ASPD), aggression, and affective disorders. A parental alcohol use disorder (AUD) may not be the proximal cause of an AUD in an adult offspring, as this condition may be due to a familial transmission of externalizing or internalizing disorders. Often, however, AUDs are correlated with ASPD. For example, a 1997 study by R. C. Kessler and colleagues determined that ASPD is found in 17 percent of alcoholic men and 8 percent of alcoholic women, compared to 3.6 percent among nonalcoholic individuals, as reported by B. F. Grant and colleagues in 2004. In a 2004 study of 1,116 twin pairs by S. R. Jaffee and colleagues, the odds of physical maltreatment were found to increase threefold when a mother or father had antisocial behavioral traits. Further, physical maltreatment predicted antisocial behavior several years later. The maltreatment was not influenced by genetic factors, and the effects of maltreatment on antisocial behavior remained significant after controlling for parental antisocial behavior and genetic transmission of antisocial behavior. This finding supports previous longitudinal studies showing that physical maltreatment plays a role in an offspring's antisocial behavior (Lansford et al., 2002; Keiley et al., 2001). Thus, maltreatment may partially explain an AUD whether an ACOA or not. In a 1997 study, T. Jacob and S. Johnson found that maltreatment, lack of affection, high levels of criticism and hostility, inconsistent discipline or supervision, and a lack of involvement can all result in aggressive, antisocial children. Likewise, maltreatment can promote deviant behavior and juvenile delinquency, and it can affect children of alcoholics and nonalcoholics similarly.

Men and women are affected differently by abuse and neglect in childhood. In a 1995 study of severely abused and neglected children, C. S. Widom and colleagues found no significant association between childhood victimization and later alcohol use in men. However, having one or more alcoholic parent predicted both *DSM-III-R* dependence criteria and an AUD. In women, a significant relationship was found between childhood abuse or neglect and alcohol-dependence criteria. Much like the men in this study, women with an alcoholic parent were significantly more likely to endorse alcohol-dependence criteria. A 2007 follow-up study found that child abuse was a significant factor for heavy drinking in middle-aged women. However, the significant effect disappeared after controlling for parental alcohol or drug problems. For men there was no significant effect of childhood abuse on later drinking behavior. This study and several others demonstrate

differential effects by gender on the relationship between a parental history of alcohol problems and the development of an alcohol problem when parental abuse is also a factor. In order to adequately study AUDs in ACOA, both parent-child and child-sibling relationships—including standardized measures of abuse and neglect—need to be taken into account.

In addition to the family dysfunction associated with parental alcoholism, a susceptibility to alcohol-use disorders in ACOA may involve shared polymorphic alcohol-metabolizing genes, a vulnerability to comorbidities, and inherited personality traits such as impulsivity and novelty-seeking. The genetic effects, when coupled with the psychosocial modeling by parents of positive alcohol expectancies and drinking behavior, result in a complex interplay of genes and environment. A family history of alcohol problems in first- or second-degree relatives is an established risk factor for an AUD, and such a history has been shown to interact with many other factors, such as expectancies about alcohol and motives for drinking.

Parental alcoholism has been linked to low self-esteem, anxiety, depression, and a perceived lack of control in ACOAs. However, adverse events in childhood may lead to resilience and improved coping mechanisms in some individuals. Studies on coping styles and resilience have been conducted to find the protective factors that might explain the heterogeneity of functioning in ACOA. Coping has been classified into two styles: approach (positive) and avoidance (negative). In a 2007 study of 128 male and female African Americans, J. C. Hall found no differences in self-esteem and coping responses between ACOA and ACONA. Hall attributes this finding to strong relationships with extended family members. However, in a 2007 sample of 209 Caucasian and African American women, M. Amodeo and colleagues found that African American women with alcoholic parents, low self-esteem, and a history of early family conflict were more likely to report avoidant coping responses.

Expectancies are beliefs about the effects of alcohol; they form early in childhood and are based, in part, on parental modeling. In 2008, A. Agrawal and colleagues completed an adult female twin study, and they found that environmental influences shape alcohol expectancies, while genetics influence motives for drinking. Heritabilities for social, coping, and conformity motives ranged from 11 percent to 22 percent. In a 2006 study of Asians, C.-Y. Hahn and colleagues found that the aldehyde dehydrogenase gene mediated the relationship between alcohol expectancies and alcohol consumption. Thus, alcohol expectancies and motivations to drink are likely to be grounded in both environment and genetics.

There is obviously still a great deal of work to be done to explain whether parental alcoholism leads directly to an increased risk of an AUD in ACOA, or whether the effects are indirect and correlated with comorbidity and maltreatment.

See also **Alcohol; Alcoholics Anonymous (AA); Treatment, Behavioral Approaches to: Twelve-Step and Disease Model Approaches.**

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CHERYL BESELER

ADVERTISING AND THE ALCOHOL INDUSTRY.

Beer and distilled spirits dominate alcohol consumption in the United States, accounting for approximately 56 percent and 30 percent of total consumption (in terms of absolute alcohol), respectively (Impact Databank, 2007). The U.S. alcohol industry is highly concentrated. Two companies—Anheuser-Busch and the merged groups SABMiller and Molson–Coors—account for approximately 80 percent of the beer sold in the United States. Ten distilled spirits companies account for 80 percent of spirits sales; the top five are responsible for 62 percent of total sales.

In a mature market dominated by large multinational alcohol marketing firms, beer and distilled spirits products are by necessity marketed products (Jernigan, 2001; Lopes, 2003). Alcohol companies spend heavily on them: In 2006, alcohol companies spent nearly $2 billion marketing alcoholic beverages on radio and television, in print, and on the Internet. According to Federal Trade Commission estimates, they spend two to three times this amount on "unmeasured" marketing activities, such as product placements, sponsorships, point of purchase advertising, on-premise promotions, and so on, for a conservative total of $6 billion per year in marketing expenditures (Federal Trade Commission, 1999).

ALCOHOL USE BY AMERICANS

In a survey conducted in 2006, 125 million Americans age twelve and older had used alcohol in the previous month (51% of the population). About 57 million people (23%) engaged in binge drinking, defined as five or more drinks on the same occasion. Of these, about 17 million Americans (6.9%) were heavy drinkers, defined as five or more drinks on the same occasion on at least five different days in the past month (Substance Abuse and Mental Health Services Administration [SAMHSA], 2007).

The percentage of college undergraduates who say they have had alcohol in the past 30 days was 65.4 percent in 2006, while 47.6 percent reported having been drunk in the past month (Johnston et al., 2007a). Among college students, 40.2 percent reported binge-drinking in the past two weeks. This is the same percentage as was reported in 1993 and 1994.

Among high school students in 2007, 15.9 percent of eighth graders, 33.4 percent of tenth graders, and 44.4 percent of twelfth graders drank alcohol in the past month, while 5.5 percent, 18.1 percent, and 28.7 percent respectively had been

drunk. The percentage of high school seniors who reported having five or more drinks in a row in the last two weeks was 25.9 percent in 2007, down from a high of 31.5 percent in 1998 (Johnston et al., 2007b).

The *Diagnostic and Statistical Manual, Fourth Edition* (*DSM-IV*) defines alcohol abuse as including one or more of the following symptoms: recurrent drinking resulting in failure to fulfill major role obligations; recurrent drinking in hazardous situations; recurrent drinking-related legal problems; and continued drinking despite recurrent social or interpersonal problems caused or exacerbated by drinking. *DSM-IV* defines alcohol dependence using seven diagnostic criteria: tolerance; the withdrawal syndrome or drinking to relieve or avoid withdrawal symptoms; drinking larger amounts or for a longer period than intended; persistent desire or unsuccessful attempts to cut down on drinking; spending a great deal of time obtaining alcohol, drinking, or recovering from the effects of drinking; giving up important social, occupational, or recreational activities in favor of drinking; and continued drinking despite a physical or psychological problem caused or exacerbated by drinking (Grant et al., 2006). According to these definitions, in 2001 to 2002, 4.65 percent of adults 18 and above were alcohol abusers, and 3.81 percent were alcohol dependent. One in four children under the age of eighteen is exposed to alcohol abuse or dependence in the family (Grant, 2000), and more than half of American adults have or have had a family member who is alcohol dependent (Dawson & Grant, 1998).

Underage alcohol use has been the subject of major reports from the National Research Council and Institute of Medicine, and the Surgeon General, who in 2007 issued the first-ever *Surgeon General's Call to Action to Reduce Underage Drinking*. Both sets of recommendations endorsed the United States' relatively high legal purchase age for alcohol of twenty-one and encouraged greater action among adults to reduce youth access to alcohol (U.S. Surgeon General, 2007).

Alcohol use is also a significant contributing factor in crime: nearly one in four (2.7 million persons) of the 11.1 million victims of violent crime reported that the perpetrator had been drinking at the time of the crime (Greenfeld, 1998). Approximately 17.6 million Americans have an alcohol use disorder, and of these 2.3 million have alcohol and drug use disorders. The relationship between the two was statistically significant for all but three of twenty-five drug use disorders studies (Stinson et al., 2006).

THE ADVERTISING PROBLEM

The high level of alcohol use by those under the age of twenty-one creates an advertising problem for the companies that market alcoholic beverages. The question for them is how to advertise to the twenty-one-and-older group and also appear not to be appealing to the under-twenty-one group. Since teenagers have a strong desire to grow up fast or at least participate in activities they view as adult, they are vulnerable to anything they believe would help them achieve adulthood.

Critics accuse the alcoholic beverage companies of making their advertising and promotional programs inviting to teenagers, who are already receptive to the ideas of engaging in adult activities, being successful, being more confident, and being more attractive to the opposite sex. The alcoholic beverage companies respond that they follow the industry voluntary advertising guidelines and do not target teenagers. They point to programs such as the public service initiatives sponsored by the U.S. beer industry, which encourage drinkers to "know when to say when," "drink smart or don't start," "think when you drink," or "drink safely." They also purchase branded "responsibility" advertising which has as its primary message drinking in moderation, safety, or not drinking before age twenty-one. Between 2001 and 2006, approximately 2.2 percent of alcohol advertising dollars on television were spent on these advertisements (Center on Alcohol Marketing and Youth, 2008).

FEDERAL OVERSIGHT OF THE ALCOHOL INDUSTRY

The U.S. Bureau of Alcohol and Tobacco Tax and Trade (TTB) in the Department of the Treasury is the federal agency with responsibility for overseeing the alcohol industry. Its rules discourage advertising claims that are obscene or misleading, as well as those that associate athletic ability with drinking. Also, the TTB takes the position that "unqualified health claims on products that pose increased health risks are deceptive." Alcoholic beverages sold in the United States have to carry

a warning on the container that states: "GOVERNMENT WARNING: (1) According to the Surgeon General, women should not drink alcoholic beverages during pregnancy because of the risk of birth defects. (2) Consumption of alcoholic beverages impairs your ability to drive a car or operate machinery, and may cause health problems."

Until the 1990s, the alcohol content of beer could not be included on the labeling of the container or in any associated advertising. As a result of a suit by Adolph Coors, a federal court decision overturned this restriction on labeling, and so companies are permitted to label their beers and malt liquors with the alcohol content. Beer averages 5 percent alcohol, ales average 6 percent, malt liquors average 4.1 percent, wine 12 percent to 20 percent, and distilled spirits from 40 percent (80 proof) to 50 percent (100 proof). Beer is usually sold in twelve-ounce containers, whereas malt liquors are usually sold in forty-ounce bottles.

The Federal Trade Commission (FTC) also reviews advertising, with emphasis on instances of false or misleading ads. At the request of Congress, the FTC issued reports on self-regulation in the alcohol industry in 1999 and 2003 (Federal Trade Commission, 2003; Federal Trade Commission, 1999). On the day that the 2003 report was released, trade associations for the beer and distilled spirits industries announced that they would tighten their standards for maximum youth audience composition of media vehicles where their members place their advertising from 50 percent to 30 percent. Since the proportion of youth ages twelve to twenty (the group at primary risk of underage drinking) is only 15 percent, the new standard still left many vehicles with disproportionate youth audiences available to alcohol advertising. In 2006, advertising in such vehicles accounted for 77 percent of youth exposure to alcohol advertising in magazines, 58 percent of youth exposure to radio advertising for alcohol, and 34 percent of youth exposure to alcohol advertising on television (Center on Alcohol Marketing and Youth, 2008).

The Food and Drug Administration (FDA) in the Department of Health and Human Services has no jurisdiction over alcohol advertising, with the exception of wines with less than 7 percent alcohol. Unlike pharmaceuticals, there is no mandate that labels or advertising materials for alcoholic products provide a list of either risks/consequences or possible health benefits. Americans regularly see ads, company logos, and billboards that encourage people to drink, but such advertising fails to provide information about the down side of drinking, especially excessive drinking.

ADVERTISING

Merriam-Webster's Collegiate Dictionary defines the verb *advertise*: "to call public attention to especially by emphasizing desirable qualities so as to arouse a desire to buy or patronize." The noun *advertising* includes "by paid announcements." The broad umbrella of advertising—in addition to television, radio, and print media—uses billboards, point-of-purchase signs and displays, and increasingly, sponsorship of special events such as music festivals; auto, bicycle, and boat racing; and other sports.

THE ROLE OF ADVERTISING

Advertising is used as a major tool in marketing. When a company first introduces a new product, the goals generally are:

1. To inform potential purchasers that a particular product is available and why they might like to try this new product.
2. To persuade people that they should go out and buy the product.
3. To let people know where the product can be purchased.
4. To reassure people who buy the product that they have made a wise choice in doing so.

When more than one company sells products in a given category, the goals generally become the following:

1. To increase market share by taking business away from a competitive product, which can be done by offering a better product or a better value and/or by increasing the level of advertising and promotion to out-shout the competition.
2. To increase the size of the market by inducing more people to start using the product. In the case of alcoholic beverages, market size increase can be accomplished by aggressively promoting features that will appeal to the potential

purchaser, that is, makes consumers more confident, more outgoing, more appealing to the opposite sex, and, in the case of minors, leads to participation in adult-type activities.

3. To increase the size of the market by inducing people to increase their usage of the product(s), which can be accomplished by tying the product to occasions such as spring break and by promoting the product heavily to the target audiences.
4. To keep reassuring heavy drinkers that they are in good company by drinking the particular brand of beer or liquor being advertised. Since the 10 percent of those who drink most heavily account for about 50 percent of all alcohol consumed in the United States, this factor is an important reason to advertise.

CORRELATION OF ADVERTISING WITH CONSUMPTION

Concern about alcohol advertising is particularly strong regarding its effects on young people. When the U.S. Federal Trade Commission looked at the issue of alcohol advertising and youth in 1999, it concluded that "while many factors may influence an underage person's drinking decisions, including among other things parents, peers and media, there is reason to believe that advertising also plays a role" (Federal Trade Commission, 1994). In 2000, a special report to the U.S. Congress on alcohol decried the lack of longitudinal studies assessing the effects of alcohol advertising on young people's drinking behavior; it concluded: "survey studies provide some evidence that alcohol advertising may influence drinking beliefs and behaviors among children and adolescents. This evidence, however, is far from conclusive" (U.S. Department of Health and Human Services, 2000).

However, the intervening six years have witnessed an outpouring of new studies, looking particularly at alcohol advertising's impact on youth. One review of the research concluded: "There is now sufficient evidence on the constituent elements of this [alcohol] marketing to say that the balance of probabilities now favours the conclusion that it is having an effect" (Hastings et al., 2005).

EFFECTS OF YOUTH EXPOSURE TO ALCOHOL MARKETING

Perhaps the most significant research development as of 2008 has been the publication of the findings of several longitudinal studies of alcohol marketing's effects on young people. One finding of these studies was that other factors such as positive expectations about alcohol use or peer effects did not predict awareness of alcohol advertising, but what best predicted awareness of alcohol advertising was actual exposure to that advertising (Collins et al., 2003) and that this awareness is evident in children as young as age nine and prevalent among fourteen-year-olds (Collins et al., 2005). All these longitudinal studies found statistically significant relationships between exposure to alcohol advertising and subsequent drinking behavior among young people. The one national study among them found that found that youth exposure to every additional alcohol ad above a monthly average of twenty-three predicted a 1 percent increase in youth drinking, while every additional dollar spent per capita on alcohol advertising in a given media market above an average of $6.80 predicted a 3 percent increase in youth drinking (Snyder et al., 2006). Other longitudinal studies found significant relationships between youth drinking behavior, on the one hand, and exposure to alcohol use in motion pictures or ownership of alcohol promotional items, on the other (McClure et al., 2006; Sargent et al., 2006).

Researchers have sought to discover how alcohol advertising affects young people's decision-making regarding alcohol use. According to one review of the neuroscience, psychology, and marketing literatures relevant to this question (Pechmann et al., 2005), understanding the biological and psychosocial context of adolescence is critical to understanding this interaction. Key to this are three distinctive vulnerabilities of adolescence: impulsivity, linked to a temporal gap between the onset of hormonal and environmental stimuli into the amygdala and the more gradual development of inhibitory control through the executive planning and decision-making functions of the pre-frontal cortex; self-consciousness and self-doubt, attributable at least in part to the emergence of abstract thinking, but evident in the greater frequency and intensity of negative mood states during adolescence; and elevated risk from product use,

including impulsive behavior such as drinking and driving, but also greater susceptibility to toxins because of the plasticity of the developing brain as well as greater sensitivity to the brain's so-called stamping functions identifying pleasure and reward. These vulnerabilities lead adolescents to be especially attracted to risky branded products that promise immediate gratification, thrills, and/or social status.

Early work on alcohol advertising and youth tended to rest on a simple theoretical basis: Exposure to alcohol advertising influences youth drinking behavior. However, subsequent studies have pointed to the importance of alcohol advertising in shaping youth attitudes, perceptions, and particularly expectancies about alcohol use, which then influence youth decisions to drink. Survey research studies on alcohol advertising and youth have found small but significant correlations between young people's awareness of this largely positive environment and drinking beliefs and behaviors among young people (Grube & Waiters, 2005).

Another question to answer concerns whether alcohol advertising targets young people. A highly contested body of research has attempted to answer the question of whether youth exposure to alcohol advertising results from intentional practices on the part of alcohol companies, or from the incidental effects of companies trying to reach a legal-aged audience. A 2003 article in the *Journal of the American Medical Association* alleged that magazine advertising by beer and liquor companies is associated with adolescent readership (Garfield, Chung, & Rathouz, 2003), but an economist who had worked as a consultant to law firms representing tobacco and alcohol interests charged that the variables in their model were too highly correlated with each other (Nelson, 2005; Nelson, 2006). Others have found, however, that this economist's own variables are too highly correlated and replicated the finding that alcohol advertisements were more likely to be placed in vehicles with disproportionately youthful audiences (Siegel et al., 2008). Others have attempted to use content analysis to assess whether alcohol advertising targets youth. They found that one of six magazine ads and one in fourteen television ads appeared to target underage drinkers (Austin & Hust, 2005).

Another concern is the effectiveness of regulatory restrictions on marketing in reducing youth drinking. One contribution to this debate examined the impact of alcohol advertising on drinking among American youth between 1996 and 1998 by combining market-level data for alcohol advertising in five media with data from two major surveys of underage drinking behavior in the United States (Saffer & Dave, 2006). Based on these data, the authors estimated that a 28 percent reduction in alcohol advertising would reduce the percentage of adolescents who drink monthly from 25 percent to between 24 and 21 percent and the percentage who engage in binge drinking monthly from 12 percent to between 11 and 8 percent.

Another study estimated the effects of several interventions—increased alcohol excise taxes; restriction of alcohol advertising; counter advertising; school-, community-, and college-based programs; family-based interventions; and interventions to prevent driving while intoxicated—on youth drinking behavior and thence on alcohol-attributable future mortality in the U.S. population. According to their analysis, the most effective intervention would be a complete ban on alcohol advertising, which would reduce deaths from harmful drinking by 7,609, equivalent to a 16.4 percent decline in alcohol-related life-years lost. A partial advertising ban (defined as a reduction in total alcohol advertising expenditures of one-third) would result in a 4 percent reduction in alcohol-related life-years lost (Hollingsworth et al., 2006).

BEVERAGE ALCOHOL PER CAPITA CONSUMPTION

In the United States, per capita consumption of all alcoholic beverages combined reached its peak in 1980 to 1981 at 2.76 gallons of pure alcohol. Per capita consumption dropped to a low of 2.15 gallons in 1995, but climbed back up to 2.24 gallons by 2005 (Lakins, Williams, & Yi, 2007). The U.S. Department of Health and Human Services has an objective for the year 2010: to reduce the per capita alcohol consumption to no more than 1.96 gallons of ethanol per person per year. However, given an increasing trend in per capita consumption since 1999, per capita alcohol consumption would need to decrease by approximately 3 percent per year from 2006 through 2010 for this objective to be met.

BEVERAGE ALCOHOL SALES

Beer ranks fourth (behind soft drinks, milk, and coffee) in per capita consumption of any kind of beverage, a position it has held for many years. Beer sales, at retail in 2004, were reported by Adams Beverage Group to be $82.2 billion, compared to $81.8 billion for soft drinks. This statistic represents 6.4 billion gallons of beer or approximately 68 billion bottles/cans of beer.

The alcoholic spirits market in 2004 tallied $49.4 billion in retail sales and totaled 394 million gallons. Wine came in third in 2004 with retail sales of $23 billion, but second by measure at 635 million gallons. The combined retail sales of all three totaled $154.2 billion (Adams Beverage Group, 2005)

THE INDUSTRY'S VOLUNTARY MARKETING CODES

Alcohol companies have answered their critics' charges by pointing to the self-regulatory codes of the three principal trade associations: the Beer Institute, the Distilled Spirits Council of the United States (DISCUS), and the Wine Institute. These codes have been expanded and strengthened in regard to placements of advertising, with both the Beer Institute and DISCUS issuing detailed guidelines regarding how the 30 percent maximum on youth audiences for alcohol advertising should be implemented and monitored. In January 2006, the Beer Institute substantially weakened the content provisions of its code. In late 2007, DISCUS issued detailed guidelines for Internet advertising. Both bodies have also improved the transparency of their code review procedures and have added third-party review processes, although the third parties involved are paid by the relevant trade associations for their work. However, there is little research evidence that content provisions of the voluntary codes are effective or enforceable. Australian researchers have examined code operations and compliance in that country and have found the self-regulatory system ineffective and fundamentally inadequate (Donovan et al., 2007; Jones & Lynch, 2007).

The issue of the correct standard for the size of youth audiences of alcohol advertising has drawn the attention not only of the Federal Trade Commission but also of state attorneys general. Attorneys general from twenty states wrote to the FTC in 2006 and requested the agency to "explore with the industry and others the reduction of the industry standard from 30 percent to 15 percent, which standard would require that alcohol advertising be limited to media where no more than 15 percent of the audience is age 12–20" (Rowe et al., 2006). A test of this lower standard using 2004 television data found that implementing it would have reduced youth exposure by 20 percent and alcohol company advertising expenditures by 8 percent, with virtually no effect on the industry's ability to reach young adults ages twenty-one to twenty-four or twenty-one to thirty-four with its advertising (Jernigan, Ostroff, & Ross, 2005).

THE COSTS OF ALCOHOL PROBLEMS

According to the U.S. Centers for Disease Control and Prevention, excessive alcohol consumption (defined as greater than 3.1 drinks per day for men and greater than 1.6 drinks per day for women) was responsible for 75,766 deaths in 2001, the latest year for which data are available as of 2008 (ARDI). According to the National Institute on Alcohol Abuse and Alcoholism, alcohol abuse and alcoholism cost an estimated $185 billion in 1998, the latest year for which estimates were available, whereas drug abuse cost the nation $148.4 billion (Office of National Drug Control Policy, 2001).

See also **Alcohol: History of Drinking in the United States.**

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ADVERTISING AND THE PHARMACEUTICAL INDUSTRY. The pharmaceutical industry, which researches, develops, produces, and markets prescription drugs in the United States, is the most heavily regulated of all industries when it comes to the advertising and promotion of its products. Through its Drug Marketing, Advertising, and Communications Divisions (DDMAC), the Food and Drug Administration (FDA) regulates all advertising and promotional activities for prescription drugs, including statements made to physicians and pharmacists by pharmaceutical sales representatives. Advertising of over-the-counter (OTC) drugs, which are not regulated by the FDA, are under the jurisdiction of the Federal Trade Commission (FTC).

Before a new prescription drug is approved for marketing, the FDA and the pharmaceutical company must agree on the "full prescribing information" that will accompany the product and that must be included in all ads, brochures, promotional pieces, and samples. This full prescribing information must include, in the correct order, the following information about the drug: its trade name, its assigned name, the strength of its dosage form, a caution statement (noting that a prescription is required), a description of its active ingredients, the clinical pharmacology of the drug, indications for its usage, contraindications for usage, precautions, adverse reactions, instructions on what to do in case of overdose, correct dosage and administration, how the drug is supplied (e.g., in pill or capsule form), and storage information. Typically, this information is very detailed, and even when it is given in six-point type, it can run to two printed pages. The pharmaceutical companies pay to have this information published in the *Physician's Desk Reference*, which is sent to U.S. medical professionals free of charge. The book is also sold in bookstores or is available on library reference shelves for use by consumers who want to know more about specific drugs.

All promotional pieces and ads used to market a new drug must first be approved by the FDA to ensure that the statements being made are consistent with those in the official labeling. After a new drug has been introduced, copies of all subsequent ads and promotional pieces must be sent to the FDA at the time of their first use, too, but they do not have to be preapproved. The FDA reviews ads, brochures, direct-mail pieces, and sales aids to ensure that they maintain a "fair balance" in presenting both the benefits and risks of a medication. In the 1990s the FDA directed its attention to scientific symposia and other medical meetings at which information about new drugs, or new indications for drugs, are presented. They ensure that the meetings are not just promotional programs for a single drug. In no other industry are advertising and promotion required to meet such strict standards.

THE CHANGING ROLE OF PHARMACEUTICAL ADVERTISING

Traditionally, companies advertised and promoted pharmaceutical products primarily to physicians, with some limited advertising and promotion being directed to pharmacists. With the expiration of

patents on some major drugs in the 1980s and 1990s, generic versions of the drugs became available from competing manufacturers. The generic drugs were priced lower than the brand-name products, so pharmacists lobbied for laws allowing them to substitute generic products for brand-name products. This gave pharmacists more control over which generic company's products to purchase and dispense. Advertising and promotion to pharmacists increased. When committees, usually composed of pharmacists, became very important in deciding which drugs could, or could not, be prescribed or reimbursed under third-party payment programs (Medicaid, HMOs, and other insurance programs), advertising and promotion were also directed to the decision makers in those organizations. Since 1981, advertising is also being directed to the consumer.

DIRECT-TO-CONSUMER ADVERTISING (DTCA)

Since the 1980s, pharmaceutical manufacturers have used DTCA to educate and foster an informed conversation between patients and their health care practitioners about health, disease, and treatments. Since the 1980s Lisa A. Foley and David J. Gross (2000) point out that DTCA comprises direct mail solicitations, radio and television commercials, magazine and newspaper advertisements, and messages on billboards and mass transit kiosks. Both the United States Government Accountability Office (2006) and Matthew Arnold (2008) show that DTCA expenditure has increased multifold from $791 million in 1996 to $4.7 billion in 2006, mainly due to the relaxation of FDA rules governing such advertisements in 1997 (The Henry J. Kaiser Family Foundation, 2001).

In addition to FDA regulations on promotional practices of the pharmaceutical industry, the member companies of the Pharmaceutical Research & Manufacturers of America (PhRMA) worked together to create a code on interactions with healthcare professionals. In addition, PhRMA established a set of voluntary guiding principles for DTCA of prescription medicines, which they posted on their Web site.

MERITS AND DEMERITS OF DTCA

DTCA is currently one of the most controversial public policy issues in the health care arena. Several claims are made about its benefits and harmful effects to society (Table 1). While proponents emphasize that DTCA informs consumers about new drug therapies and enhances patient-physician relationships, opponents state that consumers lack the expertise to assess the quality of the content of the promotional claims. Further, opponents of DTCA also believe that it will lead to increases in prescription drug costs and inappropriate health care resource utilization. In summary, stakeholders have divergent viewpoints regarding DTCA. However, studies by Barbara Mintzes (2001) and Prashant Nikam (2003) reveal that little scientific evidence exists to support hypotheses that DTCA provides potential health benefits or excludes potential harm.

DTCA AND FEDERAL REGULATIONS

The U.S. FDA regulates all prescription drug advertising under the Food, Drugs, and Cosmetic Act (US FDA CFR 202.1[e]). Prior to the early 1980s, companies did not promote prescription drugs directly to consumers. Instead, product sponsors disseminated drug information materials to healthcare professionals. In 1981 only one prescription drug was advertised to the public. By 1989, 21 pharmaceutical companies had advertised over 30 products, and estimated annual spending on consumer-directed promotion had grown to 80 million dollars. However, most advertising campaigns were disease-oriented and did not mention specific product names. The first full advertising campaign, including brand name, indication, and fine print labeling information (referred to as the "brief summary" in FDA regulations) began in 1983. Later that year the FDA asked industry to respect a voluntary moratorium on DTCA to research the impact of DTCA and to develop appropriate legislation, if required. On September 9, 1985, Kenneth R. Feather (1986) reported, the FDA ended the moratorium, stating that they had adequately studied the DTCA issue, and there was no need to provide new regulations or revise existing ones.

During the early 1990s pharmaceutical manufacturers increasingly used consumer magazines to advertise their products. These advertisements typically included a promotional message together with the brief summary of adverse effects. The brief summary appeared in small print and was not easily understood or seldom completely read by the consumers. In the 1990s pharmaceutical manufacturers

Merits	Demerits
Consumer behavior	
• Plays a valuable role in educating and informing the public about health matters and specific drug treatments • Allows consumers to participate actively in the healthcare decision making process • Improves patient-physician communication	• Confuses patients into believing that minor difference in drugs represents a major therapeutic advance; the public lacks the educational framework to judge the claims • Encourages 'doctor shopping' to obtain a desired prescription; pressures doctors to prescribe • Wastes doctors' time by having to re-educate the patients about misinformation and appropriate therapy
Healthcare resource utilization	
• Applies more appropriate use of medicines, saving lives and improving the quality of life • Encourages healthcare-seeking behavior for untreated and under treated disease states • Reduces overall healthcare costs; lowers overall drug prices due to increased competition	• Encourages inappropriate demand for medicines and/or demand for inappropriate medicines • Leads to excessive demands on physicians, over-medication, and drug abuse • Increases overall healthcare costs due to unnecessary use of expensive drugs; causes higher drug prices due to increased expenditure on drug promotion
Health outcomes	
• Leads to early symptom recognition and improved treatment outcomes • Improves compliance	• Exaggerates disease risks and promotes anxiety • Encourages 'off-label' drug use
Social and legal issues	
• Helps remove the social stigma associated with certain diseases • Increases disease and health awareness • Promotes freedom of information and commercial communication	• Creates unrealistic expectations of drugs • Takes advantage of vulnerable populations and leads to increased "medicalization" of healthy life stages • Infringes on personal privacy; weakens the learned intermediary defense, thus increasing legal liability of manufacturers

Table 1. Merits and demerits of DTCA. (Adapted from Mintzes, 2001, Nikam, 2003a.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

also started using television advertisements in a limited fashion. By the mid-1990s, product sponsors started placing "reminder" advertisements on television. These advertisements only mentioned the drug name and were extremely confusing to consumers as no health claims were disclosed.

In response to increasing consumer demand for information, the FDA began to consider regulations for broadcast (television and radio) DTCA. The FDA announced draft guidance on broadcast advertising on August 8, 1997, allowing the advertisement to omit the brief summary. Instead, manufacturers were required to state the product's major risks and provide additional sources of information (such as a toll-free phone number viewers could call to request full labeling by mail, fax, or recorded phone message; an Internet site; a simultaneous DTC print advertisement that included the brief summary; or brochures in doctors' offices, libraries, and stores). The prescription drug advertisements cannot be false or misleading, cannot omit material facts, and must present a fair balance between effectiveness and risk information. Further, the regulations specified that print advertisements must disclose every risk addressed in the product's approved labeling (US FDA FR 62:43171–43173). In August 1999 the FDA issued a final "Guidance to Industry" that specifically addressed DTCA for broadcast advertising (radio and television), but it only included minor changes to the 1997 draft (US FDA FR 64:43197–43198).

To enforce the DTC regulations, the FDA can take a variety of regulatory actions including sending letters to pharmaceutical manufacturers notifying them that they are violating the prescription drug advertisement rules. However, the number of such regulatory actions taken by the FDA has declined significantly in recent years. Wayne L. Pines (1999) and Julie M. Donohue, Marisa Cevasco, and Meredith B. Rosenthal (2007) indicate this could be either due to better compliance with promotional regulations or to a reduction in FDA oversight due to a decrease in their capacity to enforce the regulations.

DTCA IMPACT ON CONSUMER BEHAVIOR

The rate of DTCA of prescription drugs has rapidly increased from 1997 to 2006. However, only a few recent cross-sectional empirical studies (including

survey research) have assessed outcomes associated with DTCA, such as that done by Mintzes (2001). Two empirical studies showed that varying amount and format of risk information in DTCA does appear to affect consumer attitudes toward the drug advertisement in both print (Tucker & Smith, 1987) and television (Morris, Ruffner, & Klimberg, 1985). Research by William R. Doucette and John C. Schommer in 1998 also showed that variations in amount, specificity, and format of risk information had an impact on awareness and knowledge pertaining to drug-related risks. However, most studies evaluating outcomes associated with DTCA were based on observational analyses and survey-based research. Survey methodology is associated with limitations concerning the validity and reliability of responses, recall biases, and lack of ability to control extraneous variables. There is significant need for theoretically rigorous experimental research that evaluates the impact of DTCA on consumer behavior and public health.

A recent experimental study in a sample of the elderly suggests that when consumers are exposed to specific risk statements in DTC print advertisements, they were less likely to look for additional information or to adopt the advertised drug. Additionally, they held less favorable attitudes toward the advertised drug as compared to those presented with general risk statements. When risk statements were presented individually, they had no significant effect on attitudes or behaviors. However, Prashant Nikam, Dev S. Pathak, H. Rao Unnava, and Joseph F. Dasta (2003a, 2003b, 2004) found that, when exposed to four risk statements, study participants were less likely to adopt the advertised drug. Another randomized controlled trial by Richard L. Kravitz and colleagues (2005) concluded that patient's DTCA-related requests had a profound impact on physician prescribing behavior for major depression and adjustment disorder.

DTCA is one of the fastest growing forms of advertising and is expected to continue to increase because of recent FDA regulatory changes in 1997. Since the late 1990s the amount of public exposure to DTCA has significantly increased, but as Deborah J. Cook and colleagues (1992) point out, the controversy around DTCA continues to grow in the absence of credible empirical evidence meeting the scientific criteria for evaluating the quality of a study.

FUTURE OF DTCA

In 2007 healthcare spending in the United States reached $2.3 trillion, representing 16 percent of the gross domestic product (GDP) and is projected to reach $3 trillion in 2011 (Poisal, 2007, p. w243). Per projections, hospital care accounted for 31 percent, physician and clinical services 21 percent, and prescription drugs 10.3 percent of the total national health expenditure (Keehan et al., 2008, p. w146). On the pharmaceutical industry side, total spending on pharmaceutical promotion grew from $11.4 billion in 1996 to $29.9 billion in 2005. In 2005, $4.2 billion (2.6% of total sales) and $7.2 billion (4.4% of total sales) were spent on DTCA and promotion to physicians respectively. The total promotional spending, including free samples, accounts for approximately 18.2 percent of total sales revenue (United States Government Accountability Office Report, 2006, p. 13; Donohue et al., 2007, p. 676).

In the light of increasing spending on DTCA, critics charge that prescription drug advertising may lead to over-prescribing or cause pharmaceutical prices to increase, whereas advocates counter that DTCA serves an educational purpose, fosters patients-physician interactions, and assists in early detection of health conditions. On the issue of pharmaceutical pricing, empirical evidence of such a correlation is ambivalent. Overall, there is paucity of scientifically rigorous empirical research evaluating the impact of DTCA on patient-physician behavior, public health, and utilization of healthcare services.

See also **Tobacco: Smoking Cessation and Weight Gain.**

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ADVERTISING AND TOBACCO USE. Tobacco companies spend more than $13 billion annually to advertise and promote cigarettes and other tobacco products (Lindblom, 2008). The companies claim that the purpose and desired effect of marketing are to provide information and to influence brand selection among current smokers, although only about 10 percent of smokers switch brands in any one year. Because in 2007 an estimated 19.2 million adult smokers stopped smoking for at least one day during the preceding year because they were trying to quit and almost 400,000 other smokers die from smoking-related diseases, the tobacco companies must recruit thousands of new young smokers every day to replace those who die or otherwise stop smoking (Centers for Disease Control and Prevention [CDCP], 2007).

Tobacco companies contend that smoking is an "adult habit" and that adult smokers "choose" to smoke. However, medical research has clearly established that most smokers become addicted to the nicotine in cigarettes and that quitting such addiction is very difficult, according to the U.S. Department of Health and Human Services (2000).

Unlike the pharmaceutical companies, which are tightly regulated as to their advertising and promotion, the tobacco industry historically had few regulations. The basic restrictions have been that companies cannot use paid advertising on television or radio, they cannot claim what they cannot prove (e.g., that low-tar cigarettes are less hazardous to health), and they must include one of four warnings on cigarette packages and ads. The fact that warning labels are printed on a pack of cigarettes has been successfully used by the tobacco companies as a defense against tobacco victims' lawsuits.

The whole picture changed when Florida, Minnesota, Mississippi, and Texas reached an agreement in 1997 and early 1998 with the major tobacco companies and won compensation for health-care expenses incurred due to smoking. Minnesota obtained copies of long-secret memos, reports, letters, and other documents that were made public as part of the $6.6 billion settlement reached in their lawsuit against cigarette makers.

On November 23, 1998, the major tobacco companies entered into an agreement with the other forty-six states. This agreement, known as the Master Settlement Agreement (MSA), settled litigation brought by the states and other entities seeking reimbursement of expenditures related to smoking and health. Under this agreement, the states and tobacco companies jointly agreed to concrete provisions to reduce youth smoking, implement new public health initiatives, and set important new rules for governing the tobacco companies' ways of doing business.

The cigarette companies agreed to pay $368.5 billion over 25 years. Of this, $246 billion goes to the states, and they have started to receive payments under this agreement. The state of Florida receives $450 million each year under this agreement, Iowa $54.9 million, and the other states differing amounts. Iowa, Kansas, and Washington set aside this money entirely for health care. Iowa passed a law that their money will go to three areas: access to health care, public health and smoking prevention, and substance-abuse treatment and prevention. In other states, this newfound money created hot political battles over how much to spend on tobacco prevention programs.

The impact of the Master Settlement Agreement has been mixed. A 2001 study by Charles King III and Michael Siegel concluded: "The Master Settlement Agreement with the tobacco industry appears to have had little effect on cigarette advertising in magazines and on the exposure of young people to these advertisements."

A study in 2004 by Sloan, Mathews, and Trogdon concluded the MSA did no major harm to tobacco companies, and some features of the agreement may have increased company value and profitability. The report stated that profits from domestic sales rose from levels prevailing immediately before the MSA and that there was no indication that the MSA caused an increase in tobacco exports. Another 2004 study noted that whereas expected changes included reduced total expenditures and reductions for outdoor advertising, specialty promotional items identified with a brand and public entertainment used for advertising and promotions increased 96 percent between 1995 and 2001, with large increases in 1998 and 1999, as the MSA took effect. It noted that, whereas outdoor advertising declined 98 percent

between 1997 and 2001, public entertainment expenditures increased 45 percent. However, in 2001 these categories represented only a small fraction of the total budget. Of greater significance was that expenditures for retail value-added efforts increased 344 percent between 1997 and 2001 (to 42.5% of the total advertising budget), and by 2001 the incentives-to-merchants and retail value-added categories comprised more than 80 percent of total expenditures. This conclusion was supported in another study that observed large increases in promoted sales following implementation of the MSA as well as during periods of sustained cigarette excise tax increases (Loomis, Farrelly, Nonnemaker, & Mann, 2006). In 2002 the Massachusetts Department of Public Health reported that one of the smokeless tobacco companies that signed the MSA increased advertising expenditures aimed at youth by 13 percent after the agreement, although three others had decreased such advertising by 11 percent.

The MSA changed the way cigarette companies can market, advertise, and promote their cigarettes. The agreement specifically includes the following:

- No participating manufacturer may take any action, directly or indirectly, to target youth in the advertising, promotion, or marketing of tobacco products. It also prohibits any action whose *primary purpose* is to initiate, maintain, or increase the incidence of youth smoking.
- Effective April 23, 1999, billboards, stadium signs, and transit signs advertising tobacco were banned. However, this does *not* apply to retail establishments selling tobacco. They may have signs up to 14 square feet (4.3 square meters) inside or outside their stores.
- Effective May 22, 1999, the use of cartoon characters in advertising, promoting, packaging, or labeling of tobacco products was banned. (This applies only to "exaggerated depictions, or depictions of entities with superhuman powers." It does *not* cover the standard camel logo or simple drawings of a camel. It does not prohibit the continued use of the Marlboro man or other human characters.)
- Beginning July 1, 1999, participating manufacturers and others licensed by them may no longer market, distribute, offer, sell, or license any apparel or merchandise bearing a tobacco brand name.
- Free product sampling is banned anywhere, except in a facility or enclosed space where an operator can ensure that no minors are present.
- Manufacturers could not sell or distribute cigarette packs containing less than twenty cigarettes until the year 2001.
- There shall be no payment for the use of tobacco products in movies, TV programs, live performances, videos, or video games. (Does not apply to media viewed in an adult-only facility or to media not intended for distribution to or display to the public.)
- There shall be no licensing of third parties to use or advertise any brand name in a way that would constitute a violation of the MSA if done by the participants.
- No nonbranded item may be given in exchange for the purchase of tobacco products, for redemption of coupons, or for proof of purchase without proof of age.
- No use of a tobacco brand name as part of the name of a stadium shall be allowed.
- Tobacco sponsorships are limited to one per year, after a three-year grace period (from November 1998). Such brand-name sponsorship may not include concerts, events in which any paid participant or contestants are youth, or any athletic event between opposing teams in any football, basketball, baseball, soccer, or hockey league.

The previous voluntary cigarette advertising and promotion code rules are also still in effect:

1. Cigarette smoking is an adult custom. Children should not smoke. Laws prohibiting the sale of cigarettes to minors should be strictly enforced. The cigarette manufacturers may advertise and promote their products only to adult smokers. The manufacturers support the enactment and enforcement of state laws prohibiting the sale of cigarettes to persons less than 18 years of age.
2. Cigarette advertising shall not appear in publications directed primarily to those less than 21 years of age, including school, college, or university media (such as athletic, theatrical, or other programs). Comic books or comic supplements are included in this ban.

3. No one depicted in cigarette advertising shall be or appear to be under 25 years of age.
4. Cigarette advertising shall not suggest that smoking is essential to social prominence, distinction, success, or sexual attraction, nor shall it picture a person smoking in an exaggerated manner.
5. Cigarette advertising may picture attractive, healthy-looking persons provided there is no suggestion that their attractiveness and good health are due to cigarette smoking.
6. Cigarette advertising shall not depict as a smoker anyone who is or has been well known as an athlete, nor shall it show any smoker participating in, or obviously just having participated in, a physical activity requiring stamina or athletic conditioning beyond that of normal recreation.
7. No sports or celebrity testimonials shall be used or those of others who would have special appeal to persons less than 21 years of age.

The agreed-on advertising and promotional restrictions spelled out in the MSA should curb underage smoking, but tobacco companies have found ways to bypass the bans and advertise in other venues. Billboard advertising is banned, but tobacco companies have increased their level of advertising in magazines, many of which are read by teenagers.

A California suit against R. J. Reynolds Tobacco, filed on May 11, 2000, charged that the company violated the legal settlement with state governments by improperly distributing large quantities of free cigarettes by mail. This case marked the first time an attorney general took a cigarette company to court to enforce the terms of the MSA. Reynolds said it was part of a program of "consumer testing" and was therefore allowable under the agreement. The attorney general alleged Reynolds mailed the free cigarettes "under the guise of consumer testing or evaluation in order to market and advertise its products." According to the suit, Reynolds sent more than 900,000 multipack cigarette mailings to more than 115,000 California residents during 1999; some people received as many as ten packs at a time.

In his memoirs, former Surgeon General C. Everett Koop said about the tobacco industry, "After studying in depth the health hazards of smoking, I was dumbfounded—and furious. How could the tobacco industry trivialize extraordinarily important public-health information: the connection between smoking and heart disease, lung and other cancers, and a dozen or more debilitating and expensive diseases? The answer was—it just did. The tobacco industry is accountable to no one" (Koop, 1991).

WHO SMOKES?

In 2006 an estimated 72.9 million Americans aged 12 or older were current users of a tobacco product. This represents almost 30 percent of that population. In addition, 61.6 million persons (25% of the population) were current cigarette smokers; 13.7 million (5.6%) smoked cigars; 8.2 million (3.3%) used smokeless tobacco; and 2.3 million (0.9%) smoked tobacco in pipes. Young adults aged 18 to 25 had the highest rate of current use in all tobacco products, including cigarettes, compared to adults aged 26 or older. Among youths aged 12 to 17 in 2006, 2.6 million (10.4%) used cigarettes. The rate of cigarette use among 12- to 17-year-olds declined from 13 percent in 2002 to 10.4 percent in 2006. Statistics showed 2.4 million people aged 12 or older smoked cigarettes for the first time in 2006, which was similar to the 2005 estimate (2.3 million), but significantly greater than the 2002 estimate (1.9 million). Most new smokers in 2006 were under age 18 when they smoked their first cigarettes (61.2%) (Substance Abuse and Mental Health Services Administration, 2007).

UNDERSTANDING THE SMOKING HABIT

Almost all smokers started before the age of 21, most before the age of 18, and many before the age of 14. Young people who learn to inhale cigarette smoke and experience the mood-altering effects from the inhaled nicotine quickly become dependent on cigarettes to help them cope with the complexities of everyday life. Having developed nicotine dependence, they must continue smoking to avoid the downside of nicotine withdrawal. The earlier they start to smoke, the more dependent they become—and the sooner they experience smoking-related health problems. Six years of research at the National Center on Addiction and Substance Abuse at Columbia University revealed that a child who reaches age 21 without smoking, using illegal

drugs, or abusing alcohol is virtually certain never to do so. Conversely, the 2007 national survey of students indicated that more students perceive the risk of smoking but "by the time most youngsters fully appreciate the hazards of smoking, many have already initiated the behavior" (Johnston, O'Malley, Bachman, & Schulenberg, 2008).

PURPOSE OF CIGARETTE ADVERTISING

The tobacco companies are adept at using advertising and different promotional programs to help them accomplish several major objectives:

1. To reassure current smokers. To offset the effect of thousands of studies showing the adverse health effects of smoking and the requested warning labels on cigarette packages, the tobacco industry has continued to claim that no one has yet "proven" that smoking "causes" health problems—that these are just "statistical associations." But, on April 7, 2000, in Florida, a six-person jury decided that cigarettes were a "deadly, addictive, and defective product" and caused cancer for three smokers who sued the industry in a class-action lawsuit. The companies were legally obligated to award $12.7 million to the plaintiffs. In a later phase of the trial, the jury awarded $17.6 billion in punitive damages to the plaintiffs, but this ruling was contested and the case stalled in court. The state of Florida, to protect its tobacco payments in the future ultimately, passed a law capping the amount of bond the companies would have to post to appeal such punitive damages at $100 million or 10 percent of the company's net worth, whichever is less.
2. To associate smoking with pleasurable activities. In their ads, tobacco companies show healthy young people enjoying parties, dancing, attending sporting events, having picnics at the beach, sailing, and so on. The implication is that those who smoke will experience the good times enjoyed by the smokers in the ads.
3. To associate smoking with other risk-taking activities. Since as indicated by the warning labels on every package of cigarettes, smoking involves risk to one's health, tobacco companies attempt to counter this by showing in their ads such risk-taking activities as ballooning, mountain climbing, sky diving, and motorcycle riding. This is the industry's not so subtle way of saying: "Go ahead and take a risk by smoking. You are capable of deciding the level of risk you want to assume." The tobacco companies are betting on the fact that most young people consider themselves immortal and do not believe any of the negative consequences of smoking will ever affect them.
4. To associate cigarette smoking with becoming an adult. Realizing that teenagers desire to be considered adults, to be free to make their own decisions, and to be free from restrictions on what they can and cannot do, tobacco companies go to great lengths to stress that smoking is an "adult habit"—that only adults have the right to choose whether or not to smoke. Since teenagers are in a hurry to grow up and be free, the simple act of smoking cigarettes can be their way of showing to the world that they are indeed adults.
5. To associate cigarette smoking with attractiveness to the opposite sex. Many ads for cigarettes imply that if you smoke, you will also be attractive to members of the opposite sex. In fact, surveys of young people and adults show that most people prefer to date nonsmokers.
6. To associate smoking with women's liberation. "You've come a long way, baby" was the theme of the early ads for Virginia Slims cigarettes. What these ads did not say is that women who smoke like men will die like men who smoke. The slogan "Torches of Freedom" coupled with an image of women smoking cigarettes while marching down Fifth Avenue in the Easter Parade was a cigarette company's public relations ploy years ago to influence women to start smoking. In the 1990s, lung cancer became the number one cancer found in women, exceeding the incidence of breast cancer.
7. To show that smoking is an integral part of our society. The sheer number of cigarette ads—those on advertising cards, on articles of clothing, on signs at sporting events—leave the impression that smoking is socially accepted by the majority of people. This image is supported by movies that include scenes of cigarette smoking. Many events sponsored by

tobacco companies include the name of a major brand of cigarettes or smokeless tobacco, such as the Kool Jazz Festival, the Benson & Hedges Blues Festival, the Magna Custom Auto Show, the Winston Cup (stock car racing), the Marlboro Cup (soccer), the Marlboro Stakes (horse racing), and the Virginia Slims Tennis Tournament, just to name a few. Although tobacco advertising is legally prohibited on television, the ban has been ignored by the strategic placement of tobacco-product ads in baseball and football stadiums, basketball arenas, and hockey rinks, around auto racetracks, and at tractor pulls and other sporting events.

8. To discourage articles in magazines about the health risks of smoking. Ads for cigarettes, beer, food, and other products, which are marketed by the major cigarette companies or their parent companies, are so important to magazines that many publishers are reluctant to antagonize cigarette producers by running articles on the health risks of smoking. This is especially true with women's magazines.
9. To gain legitimacy. Tobacco companies seek public acceptance and recognition by supporting worthwhile groups and programs. Many groups receive significant amounts of funding from tobacco companies to support their programs. One especially large grant, from RJR Nabisco, was a contribution of $30 million for "innovative education programs" to schools across the country. In 1989 Philip Morris made arrangements to sponsor the Philip Morris Bill of Rights Exhibit, which toured the United States in celebration of the 200th anniversary of the Bill of Rights. In this way, Philip Morris tried to associate its company—including its tobacco subsidiary—with the Bill of Rights and to reap positive press coverage as the exhibit went on display in each city.

HISTORY OF TOBACCO ADVERTISING

Tobacco companies' advertising, before restrictions were implemented, focused on television, radio, newspapers, and magazines. The advertising was represented by ads such as "I'd walk a mile for a Camel" or the "Call for Phillip Morris" or "More doctors smoke Camels" or "Not a cough in a carload." This evolved into the "Joe Camel" ads, the "Kool Penguin" ads, and the "Newport Menthol" cigarette ads.

Tobacco advertising and promotional expenses have steadily increased. Advertising budgets in 2008 reached $13 billion, more than twice the expenditures of a decade before. In 1997 the tobacco companies spent $5.66 billion to promote their products, up from $5.11 billion in 1996. The largest category of spending was for promotional allowances to wholesalers and retailers, $2.4 billion, more than double their spending in 1990. Next were expenditures for retail value-added. At $970 million, this category includes non-cigarette items given away with cigarettes. Coupons and multiple pack offers were an additional $552 million, followed by specialty item distribution, $512 million; point of sale advertising, $305 million; outdoor advertising, $295 million; magazines, $236 million; public entertainment, $195 million; and $130 million for all other forms of advertising.

There were no restrictions on cigarette advertising in the United States until the first *Report of the Surgeon General* was released on January 11, 1961. Because of the health hazards described therein, the report led to the Federal Cigarette Labeling and Advertising Act of 1965 and, beginning in 1966, Congress mandated that a health warning appear on all cigarette packages, although not in advertisements. On June 2, 1967, the Federal Communications Commission (FCC) ruled that the Fairness Doctrine in advertising applied to cigarette ads on television and radio and required broadcasters who aired cigarette commercials to provide "a significant amount of time" to citizens who wished to point out that smoking "may be hazardous to the smoker's health." This rule went into effect on July 1, 1967. The FCC required that there be one free public-service announcement (PSA) for every three paid cigarette commercials. During the three-year period of 1968 to 1970, in which the PSAs were mandated by the Fairness Doctrine, per capita cigarette sales decreased by 6.9 percent.

In January 1970 the cigarette industry voluntarily offered to end all cigarette advertising on television and radio by September 1970—a move that would also eliminate any PSAs, which were hurting sales. Ultimately, Congress approved the

Public Health Cigarette Act of 1969, which prohibited cigarette advertising in the broadcast media as of January 1, 1971.

In September, the Little Cigar Act of 1973 banned broadcast advertising of little cigars (cigarette-sized cigars). During the three-year period of 1971 to 1973, following the end of the PSAs required by the Fairness Doctrine and the beginning of the broadcast advertising ban, cigarette sales increased by 4.1 percent.

More than a decade later, smokeless-tobacco advertising in the broadcast media was banned by the Comprehensive Smokeless Tobacco Health Education Act of 1986. This ban took effect on August 27, 1986. The Federal Trade Commission (FTC) Bureau of Consumer Protection ruled in 1991 that the Pinkerton Tobacco Company violated the 1986 statute banning the advertising of smokeless tobacco and prohibited it from "displaying its brand name, logo, color, or design during televised (sports) events" of its Red Man Chewing Tobacco and snuff. This was the first action of its kind by the FTC. STAT (Stop Teenage Addiction to Tobacco), at their 1991 STAT-91 Conference, addressed the problem of tobacco companies' efforts to encourage tobacco addiction in young people. It was learned that the RJR Nabisco cartoon camel was at the center of the most extensive advertising campaign ever created to influence the values and behavior of young people. Camel's share of the teenage market rose from almost nothing to almost 35 percent in just three years by using "this sleazy dromedary."

See also **Advertising and the Alcohol Industry; Nicotine; Risk Factors for Substance Use, Abuse, and Dependence: Stress; Tobacco: Dependence; Tobacco: Tobacco Industry; Tobacco: Smokeless.**

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AFGHANISTAN. Afghanistan has a long history of both medical and nonmedical drug use. Hashish and opium have been constituents of medicines prepared by *hakims* (traditional healers), and they are still used for this purpose. A tradition of hashish manufacture and use stretches back several thousand years, and opium arrived in the area over 1,000 years ago, either as a trade commodity from Egypt or Greece, where it was a popular medicine, or imported by the armies of Alexander the Great. In 1905, reports from the British Indian government noted that opium was cultivated in districts of what are now the provinces of Herat, Nangarhar, Kabul, and Qandahar. By 1932, Afghanistan was producing 75 tons of opium, although production did not start to increase significantly until the 1980s. Home-brewed alcohol was also reportedly produced and consumed in some areas, particularly the area of Nuristan, whose inhabitants were converted to Islam in 1896. While homemade wine is still produced in a few areas, this has mainly been supplanted by Russian vodka, which is illegally imported from the Central Asian Republics. Tobacco products such as *naswar*, a local form of green chewing tobacco, and proprietary brands of cigarettes are also used, contributing to health problems in a population where respiratory diseases are endemic.

TRADITIONAL USE PATTERNS

Afghanistan presents a paradox: It is a conservative Islamic country in which the use of all intoxicants is strictly *haram* (forbidden), yet cultural attitudes regarding the production and consumption of hashish, and to a lesser extent opium, has traditionally been relatively tolerant in some sections of the Afghan community. However, those who become dependent on a drug or display drug-related problems risk social opprobrium and stigma.

During the late 1960s and early 1970s, the lure of cheap and easily available hashish and opium led young Western travelers on the "hippie trail" to stay in Afghanistan while en route to India and other Eastern destinations. At the time, an Afghan psychiatrist noted that there were significant numbers of hashish users in the country, mostly from the lower classes and income groups, yet there were few associated health or social problems. He also estimated that there were around 100,000 opium addicts in Badakhshan Province, representing nearly 80 percent of the country's opiate dependent population. Many of these users originally became involved with the drug through self-medication.

WAR AND DRUGS

Thirty years of almost constant war, conflict, civil disorder, and social disruption, however, have eroded the cultural constraints and social rules that once helped to prevent occasional recreational and social drug use from lapsing into problem use and dependency. Severe impoverishment and deprivation, social displacement, loss of family members, and other war-related traumas have resulted in an increase in chronic mental health problems such as depression, anxiety and post-traumatic stress disorder (PTSD), which has led many to self-medicate with a wide range of drugs. While some use drugs recreationally (particularly hashish), and others may be influenced or coerced by peers, many use drugs simply to cope with the physical and psychological pain of daily existence.

A compounding problem is that most of the population has minimal access to reliable information on the risks and dangers of drugs, not only those traditionally available, such as hashish and opium, but also "new" drugs like heroin and a wide range of cheap and easily available psychotropic drugs, such as analgesics, hypnosedatives, and tranquilizers—particularly diazepam (Valium). In Kabul alone there are over 2,000 pharmacies where diazepam can be bought without a medical prescription for less than one dollar for a month's supply. Typically, a person will be given a medical prescription for such a drug and when this supply is finished the person will then purchase it without a prescription from a pharmacy or other shop in the bazaar. The market in psychotropics and other pharmaceuticals is largely uncontrolled and unregulated, with an estimated 80 percent of the drugs traded in the private sector being smuggled in from neighboring countries. Low-quality, out-of-date, and counterfeit pharmaceutical drugs are common.

A GROWING PROBLEM

While there are few reliable statistics in Afghanistan, all indicators and estimates suggest a substantial

increase in problem drug use since the 1970s. In 2005 a survey from the United Nations Office of Drugs and Crime (UNODC) of 1,480 key informants and 1,393 drug users in both rural and urban locations estimated that around 920,000 people, representing 3.8 percent of the population, were problem drug users. This was probably an underestimate, however, for many people who regularly use opium consider it a medicine rather than an intoxicating drug. Hidden populations of drug users—such as injecting drug users (IDUs), remote rural dwellers, police and military personnel, and female drug users—may also have been underestimated. The estimated numbers of people using drugs were: 520,000 hashish users; 180,000 pharmaceutical users; 160,000 alcohol users; 150,000 opium users; 50,000 heroin users (with 14 percent of these being injectors); and 200,000 users of other drugs, such as cough medicines, volatile liquids, and various preparations made from the cannabis plant and opium poppy capsule. Polydrug use was reportedly common, with nearly half of all drug users consuming more than one drug. A smoking mixture of opium and diazepam has also been reported in several areas of the country. This combination is popular because it prolongs the effect of the drugs and helps the user sleep better.

Injecting drug use has increasingly become a concern. In 2007 evidence from Kabul indicated that HIV prevalence among IDUs was less than 5 percent, and had thus not reached the level of a concentrated epidemic. Hepatitis C prevalence was 36.6 percent, however. High-risk behaviors are common among IDUs in Kabul, with 50.4 percent of this population sharing syringes and 76.2 percent having engaged the services of a sex worker. Similar high-risk behaviors have been reported in other Afghan cities, such as Herat and Mazar-e Sharif, where measurable IDU populations have been detected. A disproportionate number of these IDUs are returnees from Iran, where they were first introduced to heroin. A new drug designed specifically for injecting has also emerged: "crystal," allegedly a crystalline form of heroin, is reputedly easier to prepare for injecting than powder heroin, and its effects last longer.

OPIUM CULTIVATION

In general, since 1980 there has been a substantial increase in the availability of both opium and heroin, and this has been a contributing factor in the increase in problem drug use. During the 1980s and the *jihad* against the Soviet invaders, opium was cultivated to buy arms for the *mujahideen* (Afghan "holy warriors," or rebel fighters), although this was not their only source of income. While the dynamics of opium cultivation and drug production are complex, after the Soviets left in 1989, cultivation and production increased sharply, providing a source of income for many impoverished farmers and their families, for mujahideen groups (who were now fighting with each other), and for individual commanders, who used the money to expand their power base.

By 1995, when the Taliban controlled most of the country, opium production stood at 2,300 tons, and it continued to rise until 2001, when a Taliban edict banning opium cultivation dropped production to a mere 200 tons. Such a drastic decrease had the effect of further impoverishing the poorest debt-ridden farmers and increasing the price of opium, benefiting groups that held opium stocks—such as traders, traffickers, and the Taliban itself. Since 2002 and the demise of the Taliban, opium cultivation and production have increased significantly, with production in 2006 put at 6,100 tons and a record production in 2007 of 8,200 tons, with an estimated value of US $1 billion. By 2007, 14 percent of the population was estimated to be involved in opium cultivation in some capacity.

At the same time, heroin has been increasingly produced in Afghanistan, rather than over the porous eastern border in Pakistan. Large protected heroin "factories," established during the Taliban's reign, have now given way to smaller, more mobile, home-based production units. Large-scale drug bazaars have also declined, although in 2007 the Shaddle Bazaar in eastern Nangarhar province had around 30 shops trading in opium, with farmers traveling from neighboring provinces to sell their opium. Most opioids—such as opium, morphine base, and heroin—are still trafficked through Iran and Pakistan, while the rest passes through the "northern route" via the Central Asian Republics to Russia and Europe. Indicators suggest that Afghanistan's thriving drug trade has exacerbated corruption among both low- and high-level government officials, led to a building boom in several

urban areas, and funded antigovernment insurgency groups and criminal gangs.

PUNISHMENT AND TREATMENT

Under Article 27 of the Counter Narcotics Law of 2005, any person using or possessing an opioid drug or hashish for personal consumption can be imprisoned and fined. If the amount of the drug is over one gram, then penalties should also be imposed for trafficking. Paradoxically, if a medical doctor certifies that a person is addicted to a drug, the court can exempt the person from imprisonment and fine and instead order attendance at a detoxification or drug treatment center.

In reality, the weak justice system and the lack of "secure" treatment centers means that while some drug users are arrested and imprisoned, often without trial, a few attend the 40 treatment centers developed since 2002, when only two such centers existed in the whole country. Typically, these centers are underfunded, have largely unqualified and untrained staff, and are able to offer treatment and rehabilitation to only a fraction of those who need it. Most function as detoxification centers. Community-based aftercare and relapse prevention are difficult in a context of severe family impoverishment and high unemployment. Yet while drug use is seen as a criminal act, national policy now endorses the development of a wide range of treatment options, including harm reduction for IDUs, who are at risk of transmitting HIV and other blood-borne diseases.

The National Drug Control Strategy (NDCS) for Afghanistan, which was signed by President Hamid Karzai in 2003, approves treatment, rehabilitation, and harm-reduction services for individuals and families with drug problems. In May 2005 the ministers for public health and counter narcotics jointly approved the Harm Reduction Strategy for IDU and HIV/AIDS Prevention. But although such a policy framework exists for tackling drug use as a bio-psychosocial problem, there has been limited available funding for service development, and drug users are still criminalized. In Afghanistan, therefore, it is likely that, for the foreseeable future, continuing drug availability, insecurity, conflict, and impoverishment will only lead to an increase in drug consumption among many vulnerable groups, such as returning refugees, ex-combatants, the unemployed, disaffected youth, and widows.

See also **Benzodiazepines; Foreign Policy and Drugs, United States; Heroin; India and Pakistan; Injecting Drug Users and HIV; International Drug Supply Systems; Middle East; Opiates/Opioids; Opium: International Overview.**

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AFRICA. Africa is enormously diverse, with more than 900 million people living in approximately fifty countries (if surrounding island nations are included). The continent encompasses a wide-range of ecological zones, including the massive Sahara Desert in the north and the West African forest belt. These diverse ecological zones and the numerous more localized environments located within them have exerted, and continue to exert, a powerful impact on the patterns of trade and consumption of drugs and alcohol across Africa. Spread over the continent are a huge number of ethnolinguistic groups, whose cultures and belief systems often involve drug use or its proscription. In addition, much of North Africa came under Muslim control during Islam's first century, the eighth century, and spread across the Sahara and

along the East African coast. Historically, Christianity has only been important in a few areas, such as Sudan and Ethiopia, but that faith grew very rapidly during the twentieth century, as did Islam. This geographical and cultural diversity was further complicated by the expansion of international commerce into the continent and the linked colonial partition of the continent by the European powers in the decades around 1900. Beginning in the 1950s, the transition to independence or majority rule once again redefined the African map. Thus, Africa has had no common or single drug history or experience, but a multiplicity of such histories.

Each community existed within a highly articulated environment of intoxicants and stimulants, derived from locally produced or gathered agricultural products and imports. Surprisingly little research has been done on indigenous drugs other than alcohol and little is known about their histories. They had and continue to have a variety of uses, including recreational, ceremonial, and medicinal. Certainly, the boundary was not always clear between plants that might be stimulants and others that were primarily used as medicines. More recently these have been supplemented by imported crops, such as coffee and tea.

HISTORY OF ALCOHOL USE

Alcoholic drinks of various kinds were widely distributed and virtually universal, but distillation was unknown in sub-Saharan Africa before the twentieth century. African alcohols probably date at least to the introduction of grains more than 2,000 years ago. The term "beer" is used to describe these beverages, but they bear little resemblance to European-style beers. A wide range of such drinks were produced, depending on local economies and ecologies. The drinks produced from grains, honey, and fruits or from palm wine had diverse and often overlapping purposes. They were the essential lubricants on many social occasions, but the pouring of libations and ceremonial consumption had powerful ritual importance as well. As in many other areas of the world, alcohol also was often an important ingredient in medicines. Offering drinks was an inducement to labor, and in many areas tribute payments were made in the form of alcohol.

The most common forms of alcohol were drinks made from fermented grains, honey, fruit juice, sugar cane, or the liquid extracted from palm trees. The production processes differed depending on the raw materials involved, as did the division of labor involved in brewing. Women typically did most of the work involved in producing grain beers in the areas where these predominated, reflecting the central role of women in the production of these crops. They brewed millet, sorghum, and maize beers in labor-intensive methods that involved the germination of some grain to stimulate fermentation. The resulting beers were thick, porridge-like drinks, which had substantial food value. The fermentation of honey and sugar-cane juice produced thinner drinks as did the wine derived from tapping palm trees. Men generally did the work of gathering and fermenting these drinks. Maize beer only became common in the nineteenth and twentieth centuries as this imported crop spread widely. It is difficult to estimate the levels and patterns of consumption historically. Certainly all of these drinks, notwithstanding the later claims of European observers, had low alcoholic content, probably rarely exceeding four or five percent.

Strict rules generally governed the consumption of alcoholic drinks, as well as other drugs, and hierarchies typically determined drinking etiquette. At the same time, drinking also apparently provided the occasion for "time outs," in which the rules of obeisance and propriety might be suspended temporarily. Only men with considerable wealth could afford to produce grain beers on a large scale or to obtain palm wine. For most people the agricultural seasons determined the availability of drink, and only those men with the ability to amass substantial grain supplies or to command the labor to tap trees could afford to produce and distribute liquor the year round. The offering of drinks was often regarded as a critical element of generosity—an important characteristic for leaders. Among the most well-known illustrations of this phenomenon was the *odwira* festival sponsored by the King of the Asante kingdom, located in present-day Ghana. This highly orchestrated annual ritual involved a generous distribution of alcohol in gestures that reinforced the authority and stature of the king. There are many other reports of the prominent role played by alcohol in enhancing royal power, for example, in the East African kingdom of Buganda in the middle of the nineteenth century and in the Zulu kingdom in southern Africa in the 1820s.

HISTORY OF DRUG USE

The traditional alcohols produced in Africa were all in the active process of fermentation, so they could not be stored for more than a few days. As a result, extensive trades in liquor did not develop, although there were often local markets in palm wine in West African communities. In contrast, two drug products, kola and khat, could be stored and traded, although in the case of khat, only for a limited time. The kola nut was a mild stimulant harvested in the forest zones inland from the West African coast and traded to the north and east. The nut itself was not only consumed for pleasure, but its offering became a critical element in domestic hospitality. The profits from the trade were substantial, and control over it represented, for example, a crucial element in the wealth and power of the Asante king, who controlled merchant communities that monopolized the trade. The demand came largely from Muslim areas, and its popularity may have developed initially as an alternative to alcohol as communities converted to Islam.

Khat is a leafy plant chewed as a mild stimulant, again often in Muslim areas. Production centers in the Meru highlands east of Mount Kenya, from where it is distributed to communities along the Indian Ocean coast. Cannabis was also widely distributed across Africa, but seems to have been used extensively only in a few areas. At the same time, kola and khat traders took advantage of new transportation options, such as railways, trucks, and steamships, to transform the trades. Kola is a legal substance, but in the case of khat there was and continues to be official ambivalence about its acceptability.

ALCOHOL AND THE SLAVE TRADE

The expansion of international commerce with Africa introduced distilled alcohol to the continent beginning in the fifteenth century, if not before. Brandy and other spirits were mainstays of ships' cargoes from the earliest period of the Atlantic commerce, although other goods were more important in trade. With the development of the American colonies, rum emerged as a vital trade good in the transatlantic slave trade; in particular, traders used it to cement commercial deals with local middlemen and rulers along the West African coast. Further south, *aguardente*, the sugarcane liquor produced in Brazil, entered the slave trade in large quantities. Given the high cost of transport, these distilled drinks did not penetrate far beyond the coast. But in Ghana, in particular, imported rum had become deeply integrated into the social and ritual life of communities before the nineteenth century.

DRUG AND ALCOHOL ABUSE RESEARCH

Much of the earlier scholarship on precolonial or traditional African alcohol and drug use characterized such activities as "integrated" practices that reflected and reinforced social and political norms. In such circumstances social controls would make alcohol abuse virtually impossible. More recent research (see Willis, 2002) suggests that, at the very least, African communities were aware of the potential dangers associated with excessive consumption. Certainly the capacity of wealthier people to command the food resources to produce beer could undermine the food supply and accentuate hunger during certain seasons and in bad harvest years.

At the same time, the many European accounts of wild African drinking clearly reflect as much the assumptions of the observers as any objective assessment of African drinking. The perishability of fermented beers encouraged types of drinking that were typical in agricultural communities. Since these drinks had to be consumed quickly, communal beer drinks were common, and guests were encouraged to keep drinking until the liquor was finished. Thus, African concepts of moderation differed sharply from those that developed in the West, where daily drinking was the norm and the ability to hold one's liquor admired. In contrast, Africans usually drank only sporadically and often aimed at some degree of inebriation. These drinking styles probably contributed, however, to excessive drinking when alcohol became commercialized and continuously available.

INTERNATIONAL TRADE AND INTERNATIONAL CONTROL

During the late nineteenth century, the mass production of cheap gin in Holland and Germany, together with the reduction in transport costs, opened up a lucrative trade supplying *schnapps* gin to Nigeria and other areas of the West African coast—a zone where the rum trade was already established. The growth in this trade converged with the expansion of Christian missionary activity

in the region and the development of global temperance movements. As the new colonies along the coast became increasingly dependent upon the revenue derived from this trade, an active and vociferous campaign developed to challenge the so-called liquor traffic. Part of an international effort to protect indigenous peoples from the supposed ravages of the trade, for a time beginning in the 1880s, the West African liquor traffic was a major humanitarian controversy. The question was briefly discussed at the 1884 Berlin Conference, but became the focal point of the 1890 Brussels antislavery meeting.

There, in the first of a series of agreements, the major powers agreed to ban the production of spirits in tropical Africa and to ban the spread of the trade in spirits beyond those areas where it was already established. In addition, the powers increased duties on alcohol imports, purportedly to limit imports into the West African coastal region. As West African trade expanded, however, gin imports expanded as well, causing the anti-liquor trade forces to make increasingly dramatic, if largely unsubstantiated, claims regarding the destructive impact of gin imports on West African communities. Successive increased tariffs did little to stem the trade, however, and only wartime prohibition effectively reduced gin imports after 1917. This prohibition was written into international law in the 1919 Treaty of St. Germain-en-Laye, which moved beyond previous regulations to define the cheap imported gin, known as "trade spirits," as a dangerous drug, following the model of the recent international narcotics accords. The Brussels Convention had been a model for the 1911 Hague conference. Imports of more expensive spirits were still allowed, however.

The colonial regimes established in Africa beginning in the late nineteenth century passed laws that mirrored their European counterparts, gradually expanding the range of drugs declared dangerous and illegal. In contrast, their approaches to alcohol control varied. Generally, the West African colonies adopted relatively liberal approaches to liquor control, focusing attention on regulating imports but controlling locally-produced drinks through gradually expanding licensing systems. In the 1930s the first industrial breweries were established with the goal, soon realized, of creating a large African market for bottled, European beer. At the same time, a substantial illicit trade in locally produced spirits emerged. In the British colonies of eastern and central Africa as well as in South Africa, Africans were forbidden entirely to consume spirits; European beer and wine were also prohibited. In those areas, regulation focused on controlling production and consumption of traditional African beers, although some of it was now commercially produced. Although household production continued relatively unimpeded in rural areas, in cities throughout most of the region, beer sales were confined to state-owned establishments, which produced substantial revenues for the state. In fact, one of the obvious themes in the history of the alcohol commerce in Africa is its close tie to state revenue, a tie that has possibly become even stronger in the twenty-first century.

The period of decolonization brought gradual liberalization of alcohol regulations and, with independence and majority rule, all elements of racial discrimination in alcohol distribution were eliminated. Independence also brought a rapid increase in levels of production and consumption as well as the emergence of large-scale and powerful brewing and distilling concerns, many of which had ties both to international liquor capital and to the state. The expansion of production and consumption also brought increased public health concern about excessive alcohol use, and denunciations of drunkenness became mainstays of political discourse in many countries. Few countries had the resources to devote to treatment facilities, and alcohol experts conceptualized African drinking and alcohol abuse in collective terms, an approach at odds with the individualized disease models that predominated in the West. The newly independent governments also generally followed the lead of the United States in the adoption of severe restrictions on illegal drugs and harsh penalties for drug trading and possession.

CANNABIS PRODUCTION AND USE

Cannabis production is widespread in Africa and has expanded substantially since the 1960s. There is a surprising dearth of information on what is increasingly a major crop, reflecting perhaps the dangers of researching a trade that is illegal, but involves the complicity of many state officials and

legitimate businesspersons. It is estimated that by the 1990s 15 percent of the population of Ghana were regular users of cannabis, but that 50 percent of the local crop was exported to other African countries and to Europe. The decline in the 1980s of markets for many of Africa's key agricultural resources created the economic context for a shift to cannabis production in a number of countries in addition to Ghana, because the crop produced healthy profits even when the costs associated with illegal activity were considered. At the same time the general economic decline provided both a ready supply of transporters and dealers and a growing market.

Consumers typically fell into two categories: those who used the drug for pleasure and those who used it because of strenuous or stressful work. An extreme example of this is the systematic provision of cannabis and other drugs to the "boy soldiers" and other combatants in the civil conflicts in Sierra Leone, Liberia, and other countries. Through the 1980s cannabis entirely dominated the African drug economy, but beginning in the 1990s the use of imported drugs became much more common. Predictably, the growing role of African countries in international drug trafficking has attracted much more interest from scholars and the news media than the production and distribution of drugs within Africa itself.

INTERNATIONAL TRADE IN ILLEGAL DRUGS

Before the 1980s Africa did not usually surface in discussions of international drug trafficking. With its close proximity to Spain, Morocco had developed a substantial cannabis production industry and exported the product, especially in the form of hashish, across North Africa and into Europe. During the late 1980s and early 1990s, however, a number of African countries became involved in the global drugs trade. In some cases, for example Ghana and especially Nigeria, local entrepreneurs built substantial international trading enterprises. In other cases, external cartels built connections with local interests, as the international trade shifted and diversified to maintain profits. Initially, African countries were largely transit points, funneling drugs produced elsewhere to markets in Europe and the United States.

In these circumstances it was often difficult to attract the political support and resources to attack the trade. Occasionally, African commentators even noted an ironic reversal, in which the continent that had been exploited by external powers was now profiting from a vast commerce that ultimately fed on demand largely concentrated in the former imperial states. By the late 1990s, however, the transit trade had begun to spill over into local cultures and economies, and the drugs trade became a hot button political issue.

In a number of key respects, African countries were fertile ground in the 1980s and 1990s for the development of drug trafficking. Colonialism had bequeathed economies highly oriented toward production for export and dependent on foreign investment. The economic downturn of the late 1970s had a devastating impact across the continent, as country after country was forced into structural adjustment programs to encourage more open economies and reduce the state role in the economy. Whatever the long-term impact of such programs, in the short run unemployment and under-employment grew rapidly, and the ranks of the desperately poor expanded. Increasing numbers of formerly middle class and educated people found themselves living hand to mouth, with few prospects. Migration to towns and cities accentuated these problems, as a formerly overwhelmingly rural continent became urbanized.

Structural adjustment policies resulted in reductions in government expenditures, and weaker states were unable to combat increasingly sophisticated drug syndicates. Impoverished bureaucracies and officials were highly susceptible to corruption in environments where ineffectual state regulation made money laundering and evasion of customs relatively easy. In many countries, privatization and democratization accentuated a shift toward a culture of private entrepreneurship that sometimes ignored illegality. In an extreme example, West Africans have established their own international drug distribution concerns and have become important players in the global drug trade. In this environment, unfortunately, drug policies on the continent have been driven as much by United States pressure as by the assessment of local needs and realities. It is a sobering fact that the international economy has produced heroin at prices that are within reach of addicts in poor African communities along the East African coast and elsewhere, but cannot deliver cheap pharmaceuticals that would combat epidemics of HIV and malaria.

See also **Alcohol: History of Drinking (International); Foreign Policy and Drugs; International Drug Supply Systems; Kenya; Khat; Nigeria; South Africa.**

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CHARLES AMBLER

AFRICAN AMERICANS, ETHNIC AND CULTURAL FACTORS RELEVANT TO TREATMENT FOR.

Leading experts (Helms & Cook, 1999; Pinderhughes, 1989) defined ethnicity as the historical cultural patterns and the collective identity shared by groups from specific geographic regions of the world, and culture is defined as the commonly shared beliefs, values, and norms of groups. Sufficient evidence (Jones-Saumty, 2002; Mallow & Cameron-Kelly, 2006) supports the importance of cultural congruency or competency in substance abuse treatment with ethnically and culturally diverse populations. Cultural congruency is synonymous with cultural competency, a widely recognized term in mental health care. Cultural competency assumes that mental health providers should possess knowledge and skills of a particular culture to deliver effective interventions to members of that culture. Three areas generally determine cultural competency (Sue, 2006): (a) Cultural awareness and beliefs: Providers' sensitivity to their own personal values and biases and how these may influence perceptions of the client, client's problem, and the counseling relationship; (b) Cultural knowledge: Counselor's knowledge of the client's culture, worldview, and expectations for the counseling relationship; and (c) Cultural skills: Counselor's ability to intervene in a manner that is culturally sensitive and relevant.

BACKGROUND

African Americans are an ethnically and culturally diverse group, and their cultural values and norms reflect this diversity. Historically, many of the cultural values and norms shared by African Americans have been shaped by the experiences this group has had from slavery to contemporary society. Racial pride and identity are values passed down from generation to generation along with socialization skills that serve as the foundation for the development and survival of African Americans in the United States.

Moral codes of behavior are primarily derived from enduring spiritual and religious beliefs and practices that influence individual character and collective interactions. Moreover, African Americans express firm ties to family whether biological or surrogate, social support networks, and even in the early twenty-first century, remain consistent in their communal aspects of daily existence. For example, in Black religious organizations the term *church family* is often used; or, when individuals are in treatment, fellow program participants are

viewed as a *recovery family*, with whom aftercare support relationships are created.

African Americans have demonstrated flexibility in altering certain cultural values and norms when adapting to different needs and demands of the group and society. For instance, research by Neighbors and colleagues (2007) documented increases in access to and utilization of mental health treatment and substance abuse treatment services, which shows that African Americans have progressively evolved in attitudes and behavior about these services.

Periodically, notable cultural issues and drug use trends impact how African Americans view and respond to treatment. The crack epidemic is a prime example. The crack epidemic emerged during the late 1980s, and a number of African American communities experienced its devastating effects. Many African Americans addicted to crack made a marked departure from traditional cultural values and norms indicated by a rise in risky sexual behaviors and diseases, dramatically altered family lifestyles, a sharp increase in criminal activity and violence, and weakened and sometimes dismantled community cohesiveness.

Crack dependency introduced different members of the African American community into the mental health and substance abuse treatment systems. Researchers and treatment providers responded slowly to the crack crisis, but eventually these efforts accelerated and intensified. The result was that drug treatment demonstrated more interest in culturally based approaches for minority groups, and treatment services tailored for the growing number of women who abused crack also grew. This coordinated response to the crack epidemic remained active into the early twenty-first century and is an indication that attention to cultural issues and drug use trends and treatment patterns must be an ongoing process.

TREATMENT PATTERNS

As treatment data from the Substance Abuse and Mental Health Services Administration-Drug and Alcohol Information Services (SAMHSA-DASIS) revealed in 2002, African Americans as a group usually sought and received treatment services for both illicit and legal chemical dependency. According to data from the 1999 Treatment Episode Data Set (TEDS) and DASIS report, although non-Hispanic Blacks made up 12 percent of the U.S. population in 1999, this group represented 23 percent of admissions to publicly funded substance abuse treatment facilities (SAMHSA-TEDS, 2006).

Treatment seeking and utilization patterns of African Americans must be assessed on both an individual and community-wide basis. The idea that African Americans are a homogenous group is flawed. For example, Waggoner and Brinson (2007) documented differences in rates of drug use trends and treatment patterns for rural and inner-city dwellers along with emerging data on ethnic intergroup variability in treatment utilization.

Despite the non-uniform character of African Americans as a group, most still manifest resistance to drug treatment. The National Survey on Drug Use and Health (NSDUH) provided information on the general population's five most often reported reasons for not receiving illicit drug or alcohol use treatment. Although this report did not indicate specific data on any particular ethnic group, it is still useful information when applied to African Americans. This information may provide insight into why African Americans do not seek treatment (2006).

This report, based on combined data of 2004 to 2006, gave an overview of persons who needed, but did not receive, treatment at a specialty facility and their perceived need for treatment. The five main reasons for not seeking treatment were: (a) not ready to stop using (37.2 percent); (b) no health coverage and could not afford cost (30.9%); (c) possible negative effect on job (13.3%); (d) not knowing where to go for treatment (12.6%); and (e) fear of neighbors' or community's negative opinions (11.0%) (SAMHSA-NSDUH, 2006).

POST-TREATMENT SUPPORT: RECOVERY GROUP PARTICIPATION

African Americans participate in substance abuse recovery or mutual-help groups, but the exact type and rates of participation can only be roughly estimated as an independent source of data was not found. In general, of the four million persons aged 12 or older (1.6% of the population) who received treatment for a problem related to the use of alcohol or illicit drugs in 2006, more than half (2.2

million) received treatment at a self-help group (SAMHSA, 2006).

The two categories for aftercare drug treatment and recovery groups are traditional and non-traditional/alternative. The most common traditional recovery groups are Alcoholics Anonymous (AA) and Narcotics Anonymous (NA). These two groups are based on the twelve-step philosophy of the individual's spiritual awareness of a higher power and admission of powerlessness over the substance(s). Alternative drug recovery groups (e.g., women- or health-specific) similar to these traditional ones are modeled after the self-help movement, which encourages personal responsibility and action to prevent relapses.

African Americans utilize both traditional and alternative drug recovery and relapse prevention groups; however, participation at mutual-help groups has a different meaning and outcome for them because of cultural factors such as segregation and racism. In 1993 Smith, Buxton, Bilal, and Seymour attributed African Americans' resistance to the twelve-step model to the perception that these fellowships were exclusive; some also confused them with religion, and confusion over surrender versus powerlessness was also an issue. Other concerns included low self-esteem, dysfunctional family structure, communication difficulties, and institutionalized and internalized racism.

CULTURAL RISK AND PROTECTIVE FACTORS

African Americans have multiple cultural risk and protective factors that influence patterns of substance abuse as well as the type and quality of treatment received. Research by Terrell (1993) suggests that acculturation experiences, sources of stress, coping mechanisms, social support variations, and beliefs about substance use are key factors associated with differential patterns of substance abuse among some ethnic groups, particularly African Americans, Hispanics, and Native Americans.

Cultural strengths and barriers promote or impede treatment utilization and outcomes for substance abusers. For example, they may be encouraged or discouraged by peers, spiritual leaders, or circumstances to deny the need for treatment or to change drug-using lifestyles once in treatment. Furthermore, there is a growing recognition that for maximum engagement of women in treatment, providers must have an understanding of sociocultural factors, gender needs and differences, and an awareness of childhood problems some women may have experienced, including childhood sexual and/or physical trauma.

The most prominent ethnocultural factors that have an impact on substance abuse treatment for African Americans include personal or individual motivation, education/employment/economics, religion/spirituality, family/social support, racism (internal and external) including diversity and cultural identity, neighborhood/environment, and legal criminal justice status. A summary of these factors follows.

Motivation. Motivation for drug use treatment is widely regarded as crucial to a client's engagement in treatment and also in success in quitting drug use. Motivation is typically measured with items reflecting high treatment readiness (e.g., perceived need for treatment and commitment to participate) and low treatment resistance (e.g., skepticism regarding benefits of treatment).

MET or Motivational Interviewing (MI) is an approach wherein motivation to change substance use can be achieved by increasing individual awareness of negative consequences using a nonconfrontational approach. Motivation can affect treatment retention results for specific drug users and types. Cocaine-dependent patients (African Americans accounted for less than 10% of the sample) with low initial motivation to change reported less cocaine and alcohol relapse and use days and fewer alcohol problems than Motivational Enhancement Therapy (MET) patients with higher initial motivation. One possible explanation for this phenomenon, offered by the authors of the study, is that the more permissive message used in MET is maladaptive for the more motivated patients who may respond to a more directive approach.

Education/Employment. Education and employment status are also important factors for marginalized substance abusers. Among substance abusers admitted to treatment for illicit drug use (2003–2004), a significant number of African Americans had at least a high school education (SAMHSA-NSDUH, 2006). A study of treatment retention for urban, uninsured, adult African Americans in substance abuse treatment done by Mitchell

Hampton (2006) shows that education did not have any significant influences on retention other than an indication that those with higher levels of education are likely to stay longer.

Employment has no significant relation with retention, although studies indicate that employed people, full-time or part-time, tend to stay longer than those who are unemployed. The majority of U.S. adults with substance abuse or dependence problems, however, are gainfully employed. Research data on employment status and trends for African American substance abusers are limited and, when included, the numbers are extremely low. For example, in a 2006 study by Slaymaker and Owen on employment status of substance abusers in treatment, the sample size for African Americans was negligible (less than 3%).

The available research (Brown, Melchior, Slaughter, & Huba, 2005) was based on African American women, and the cultural implications of this should be considered by researchers. Employment was one of three indicators that women (66.3% African American) seeking to enter substance-abuse treatment were ready to modify several types of risky behaviors. Other indicators are seeking mental health counseling, reducing risky sexual behaviors, reducing risk of physical violence, and improving vocational or educational skills. Results demonstrated that, when these factors were present, significant increases occurred in women's readiness for behavior change. The interaction between initial readiness to modify substance-abuse behaviors and longitudinal change also was significant.

Religion and Spirituality. Religion and spirituality play a significant role for African Americans seeking drug treatment. Religion is an organized social system of beliefs and practices, whereas spirituality refers to an individual's unique, subjective sense of meaning and/or transcendent experiences. Religion can produce positive higher resolve to consume less drugs, or it can cause distress when struggling to make independent choices.

In 2007 Michalak, Trocki, and Bond investigated the relative importance of three religion variables (religious preference, religiosity, and alcohol proscription) and eight demographic variables (gender, ethnicity, education, income, marital status, age, region, and employment status) as predictors of drinking versus abstention and moderate versus heavy drinking in a representative racial sample. Religion variables were strongly associated with abstention in that study.

Likewise, religion and spirituality is strong for African Americans regardless of gender. Heinz, Epstein, and Preston reported that women and African American heroin and cocaine abusers were more likely to report religious and spiritual beliefs or experiences on several individual religion-based items than men and non-African Americans (2007). African Americans had higher scores on the Index of Spiritual Experience (INSPIRIT)—a questionnaire that assesses both spirituality and religiosity—than Caucasians. These findings suggest that spiritual and religious experiences in substance-abuse recovery, along with demographic characteristics, should be considered in the design of spiritually oriented behavioral interventions for addiction.

Family and Social Support. The majority of African Americans have strong connections to family and social support networks that directly influence both positive and negative treatment outcomes, but gender differences exist. For example, the leading referral source of African American males is the criminal justice system, whereas for females it is self or a family member (SAMHSA, 2006). Unfortunately, most mental health facilities still lack family education services.

Racism: Internal and External. African Americans cope with racism both internally and externally. The difficulty of dealing with both of these stressors is perhaps amplified for substance abusers. External racism or oppression has been strongly correlated with race-related stress and negative emotional reactions. Internalized racism is a form of racial hatred associated with poor mental health outcomes such as low self-esteem and depression. Institutional racism occurs but is often hard to identify; nevertheless, it is felt by many who still believe that white society is "out to get them," a central longstanding idea in the so-called *conspiracy theory*. The prevalence of conspiracy theories among African Americans is associated with the historical patterns of systematic discrimination and racism from slavery to the Jim Crow laws in the South to the current

disenfranchisement and inequities such as those found in the criminal justice system.

Understanding and integrating diversity and recognition of cultural identity needs will help break down barriers to effective treatment and research on substance dependence. One large study (Jacobson, Robinson, & Blumenthal, 2007) on racial disparities examined intake and discharge records from all publicly funded outpatient and residential alcohol-treatment recovery programs in Los Angeles County during 1998 to 2000. Study participants (N = 10,591) were African American, Hispanic, and white patients discharged from these programs, ages 18 or older, who reported alcohol as their primary substance abuse problem. African Americans had significantly lower completion rates (17.5%) relative to whites (26.7%). These large differences in completion rates between African American and white patients are partially explained by economic differences (i.e., employment, homelessness, and usage of Medi-Cal rather than private insurance), but these factors remain largely unexplored.

Legal/Criminal Justice Status. Frequently, the judicial system will use legal coercion to provide treatment to substance users, with the expressed intent of diverting them from incarceration. Legal or criminal justice involvement of African Americans with substance abuse problems is considered a typical outcome for this ethnic group, but the system is often seen as unfairly biased against them.

The question is: How effective is mandated treatment for this population? The answer is mixed. Perron and Bright found that legal coercion reduced the risk of dropout across three treatment modalities—short-term residential, long-term residential, and outpatient (2008). Alternatively, in a sample that was 60.7 percent African Americans, 33.5 percent non-Hispanic Whites, and 21.2 percent women whose ages ranged from 16 to 63 years old, readiness (but not resistance) predicted treatment retention during the six-month period. Resistance (but not readiness) predicted drug use, especially among offenders for whom the treatment referral was coercive. These findings suggest that readiness and resistance should both be assessed among clients entering treatment, especially when the referral is coercive.

Neighborhood/Environment. The link between poor health outcomes such as depression and other psychiatric disorders, substance abuse, and the quality of neighborhoods and environment of African Americans has been firmly established. Many African Americans must contend with the marketing of substances, living in high-stress environments (e.g., low income, crime-ridden, high unemployment areas), and other risk factors. The interface of addiction and treatment in this context is equally disturbing. Society expects oppressed groups to seek help from social institutions where alienation and segregation is perceived as the norm. This inherent contradiction and the mistrust generated by perceived and real racism often results in underutilization of treatment services by this group even when such services are available.

CULTURALLY CONGRUENT TREATMENT MODELS

For successful engagement and retention of clients, providers of treatment programs need to understand the role that culture plays in the daily lives of African Americans. As previously discussed, multiple ethnocultural factors contribute to the success or failure of treatment. Treatment models that use this information offer African Americans with substance abuse problems diverse program options. Two culturally congruent substance-abuse-treatment models are the African American Extended Family Program and the Sande Society.

The African American Extended Family Program is a good example of how the precepts of twelve-step recovery can be adapted to the needs of a specific community. It takes African American cultural mores and traditions into consideration and makes them primary to recovery. Culturally, African Americans strongly value communalism, or a collective identity (Longshore & Grills, 2000). The Haight-Ashbury Free Clinics, Inc. (HAFCI)/Glide Memorial Methodist Church African American Extended Family Program (AAEFP), described in detail in Reverend Cecil William's book, *No Hiding Place*, offers this family program. This program represents an important collaboration that has established an effective intervention in the inner-city crisis of crack-cocaine use. This intervention is an adaptation of the traditional twelve-step principles of supported recovery for African

American inner-city culture. In the *HAFCI-Glide* program, the basic practicalities of recovery are utilized in a model that is uniquely meaningful in terms of the African American experience.

The Big Book of Alcoholic Anonymous (AA) uses the terms *spiritual experience* and *spiritual awakening*, manifesting in many different forms, to describe what happens to bring about a personality change sufficient to induce recovery. While some of these may involve an "immediate and overwhelming God consciousness," most are what William James called an "educational variety" of revelation, developing slowly over time. According to a *Big Book* appendix titled "Spiritual Experience," the core of this process is tapping an "unexpected inner resource" by members who identify this resource with "their own conception of a Power greater than themselves." African-centered approaches offer an alternative conceptual framework for understanding the culturally normative behavior of African Americans in drug abuse treatment and recovery. They are based on an appreciation of core African-centered beliefs. The program developers proposed seven fundamental constructs to serve as the basis of a model for African-centered transformative healing: consciousness, character, conduct, collectivity, competence, caring, and creed.

The Sande Society is another example of an African-centered substance abuse program. It is a *rite-of-passage* approach involving highly developed ritual based on that of the Bundi society in Sierra Leone. This treatment approach with its African-centered themes was developed with special consideration for holding together and rebuilding the families of African American women. This program integrates four treatment phases (each four months long) linked to four principles for a balanced life: (1) *Genesis/Restraint*; (2) *Initiation/Respect*; (3) *Transformation/Responsibility*; and (4) Sande Society/Reciprocity. These are the basis for participants and family members to make personal life changes and to grow mentally, spiritually, and physically healthy.

Family preservation is a primary factor in this treatment process. The communal environment has individual apartments equipped with kitchens, communal group and meeting rooms, a fully equipped childcare center, a recreational and exercise gym, a vocational training room, a medical/health area, and staff offices. It promotes positive social interactions between families and decreases isolation and functioning outside the collective. Ultimately, Sande Society members participate in sharing their experiences and stories of challenges and success in supportive empowerment and teaching sessions.

SUMMARY

Ethnic and cultural factors relevant to substance abuse treatment for African Americans are complex and require constant review. African Americans, similar to other ethnic and cultural groups, have specific cultural values and norms regarding treatment for substance abuse. Researchers and treatment providers need to understand and integrate relevant ethnocultural factors in the development of effective culturally congruent interventions. This specialized information when combined with scientific data on drug-use trends and treatment patterns has the potential to improve treatment utilization and outcomes for this population. While significant progress is evident in the ethnoculutural attitudes and behaviors of African Americans regarding treatment for substance abuse problems, more emphasis should be placed on the development of community-based prevention and outreach efforts. Culturally-based treatment appears to be making some progress with African Americans. The immediate challenge to researchers and treatment providers is to establish evidenced-based treatment models and to demonstrate the effectiveness of the programs for African Americans.

See also **Alcoholics Anonymous (AA); Coerced Treatment for Substance Offenders; Crack; Ethnopharmacology; Gender and Complications of Substance Abuse; Narcotics Anonymous (NA); National Survey on Drug Use and Health (NSDUH); Prevention; Religion and Drug Use; Risk Factors for Substance Use, Abuse, and Dependence: Gender; Risk Factors for Substance Use, Abuse, and Dependence: Race/Ethnicity; Treatment, Behavioral Approaches to: Self-Help and Anonymous Groups; Treatment, Behavioral Approaches to: Twelve-Step and Disease Model Approaches; Treatment, Stages/Phases of: Aftercare; Treatment: An Overview; U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA); Welfare Policy and Substance Abuse in the United States.**

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CARLEEN ROBINSON
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AGGRESSION AND DRUGS: RESEARCH ISSUES. Alcohol, more than any other drug, has been linked to aggressive and violent behavior. Alcohol, opioids, hallucinogens, and psychomotor stimulants differ markedly from each other in terms of their pharmacology and neurobiological mechanisms, dependence liability, legal and social restraints, expectations, and cultural traditions. Each of these substances triggers, escalates, and disrupts aggressive behavior via distinctly different mechanisms, and it would be misleading to extrapolate from the conditions that promote violence in individuals under the influence of alcohol to those with other drugs. Different types of drugs interact with aggressive and violent behavior in several ways including (1) direct activation of brain mechanisms that control aggression, mainly in individuals who have been aggressive in the past; (2) drug states, such as alcohol or hallucinogen intoxication, serving as license for violent and aggressive behavior; (3) drugs such as heroin or cocaine serving as commodities in an illegal distribution system, drug trafficking, which relies on

violent enforcement tactics; and (4) violent behavior representing one of the means by which an expensive cocaine or heroin habit is financed. Systematic experimental studies in animals represent the primary means to investigate the proximal and distal causes of aggressive behavior, whereas studies in humans most often attempt to infer causative relationships mainly by correlating the incidence of violent and aggressive behavior with past alcohol intake or abuse of other drugs. The ethical dilemma of research on aggression in animals and humans is the need to reduce harm and risk to the research subject, on the one hand, and on the other, to capture clearly the essential features of human violence, which is by definition injurious and harmful.

HOW TO MODEL VIOLENT BEHAVIOR IN EXPERIMENTAL RESEARCH WITH ANIMALS

Methodologically, aggression research stems from several scientific roots, the experimental-psychological, ethological (focusing on the evolutionary biology of behavior), and neurological traditions being the most important. The use of aversive environmental manipulations to produce defensive and aggressive behavior has been the focus of the experimental-psychological approach. During the 1960s models of aggression were developed that rely on prolonged isolated housing or crowding; exposure to noxious, painful electrical shock pulses; omission of scheduled rewards ("frustration"); or restricted access to limited food supplies as the major aversive environmental manipulations. The behavioral endpoints in these models are defensive postures and bites in otherwise placid, domesticated laboratory animals. Animal models of aggressive behavior become relevant to the human condition when they successfully capture the escalated nature of aggressive behavior such as after social provocation and after frustrating experiences. Aggression research using human subjects studied under controlled laboratory conditions has employed aversive environmental manipulations, such as the administration of electric shocks, noxious noise, or loss of prize money to a fictitious opponent. This type of experimental aggression research highlights the dilemma of attempting to model essential features of violence under controlled laboratory conditions without risking the harm and injury that are characteristic of such phenomena. Because it is unethical to conduct experimental studies that involve realistic violent behavior, competitive behavior in laboratory situations is often used to model violence in the laboratory. However, the validity of this model to violence in the real world has rarely been tested.

In addition to environmental manipulations, histopathological findings of brain tumors in violent patients prompted the development of experimental procedures to destroy tissue in areas of the brain such as the septal forebrain, medial hypothalamus, or certain midbrain regions of laboratory rats and other animals. Such experimental manipulations most often result in rage-like defensive postures and biting, often called rage, hyperreactivity, and hyperdefensiveness. Alternatively, electrical stimulation of specific brain regions can evoke predatory attack, and aggressive and defensive responses in certain animal species. When animals are given very high, near-toxic doses of amphetamines and similar drugs, bizarre, rage-like responses may emerge. Similarly, aggressive and defensive behavioral elements are induced by exposure to very high doses of hallucinogens and during withdrawal from opiates. The inappropriate context, the unusually fragmented behavioral response patterns, and the inclusion of only domesticated laboratory rodents make aggressive and defensive reactions that are induced by lesions, electrical brain stimulation, drugs, and toxins difficult to interpret or generalize to the human situation.

In contrast to the emphasis on aversive environmental determinants or on neuropathology, the ethological approach to the study of animal aggression has focused on adaptive forms of aggressive behavior. Defense of a territory, rival fighting among mature males during the formation and maintenance of a group, defense of the young by a female, and antipredator defense are examples of these types of aggressive, defensive, and submissive behavior patterns, often referred to as agonistic behavior.

Sociobiological analysis portrays these behavior patterns as having evolved as part of reproductive strategies ultimately serving the transmission of genetic information to the next generation. The focus on aggressive behavior as it serves an adaptive function in reproductive strategies, however, complicates the extrapolation to violent behavior as it is defined at the human level. How the range of

human violent acts relates to the various types of animal aggression and how it may share common biological roots remain to be specified.

ALCOHOL

How have these ethological, neurological, and experimental-psychological research traditions contributed to our understanding of the link between drugs of abuse and alcohol to human aggression and violence? Epidemiological and criminal statistics link alcohol to aggressive and violent behavior in humans. The pattern of this association is large in magnitude, consistent over the years, widespread in the types of aggressive and violent acts, massive in cost to the individual, family, and society, and serious in the suffering and harm caused. Systematic experimental studies have identified the early phase after a low acute (short-term) alcohol dose as a condition that increases the probability of many types of social interactions, including aggressive and competitive behaviors, and high-dose alcohol (with intoxication) as the condition most likely to be linked to many different kinds of violent activities. Yet, most alcohol drinking is associated with acceptable social behavior. This is because individuals differ markedly in their propensity to become intoxicated with alcoholic beverages and subsequently to engage in violent and aggressive behavior, rendering population averages poor representations of how alcohol causes individuals to behave violently. The sources for the individual differences derive from interactions among genetic, developmental, social, and other environmental factors. Genetic association between antisocial personality, possibly diagnosed with the aid of certain electrophysiological measures, and alcoholism remains to be firmly established.

In the early 1990s the neurobiological mechanisms of alcohol action for a range of physiological and behavioral functions began to be identified; it appears that the actions of alcohol on ionophoric (regulating the movement of ions into the neuron and its action potential threshold) serotonin, glutamate, and GABA receptor subtypes are particularly relevant to alcohol's effects on aggressive and violent behavior. For example, studies in rodents and primates indicate that subtype-selective benzodiazepine-receptor antagonists prevent the aggression-heightening effects of alcohol. Molecular mutations of GABA receptor subunits provide further insight into the mechanisms via which alcohol heightens aggressive behavior in certain individuals. Similarly, the actions of alcohol on neuroendocrine events that control testosterone and adrenal hormones appear important in the mechanisms of alcohol's aggression-heightening effects. Among the environmental determinants of alcohol's effects on violence that are of paramount significance are social expectations and cultural habits as well as the early history of the individual in situations of social conflict. Impaired appraisal of the consequences, inappropriate sending and receiving of socially significant signals, and disrupted patterns of social interactions are characteristics of alcohol intoxication that contribute to its violence-promoting effects. A particularly consistent observation is the high prevalence of recent alcohol ingestion in victims and targets of aggression and violence. In contrast to heroin and cocaine, because alcohol is not an illicit drug, its link to violence is not a characteristic of the economic distribution network for this substance.

OPIOIDS

Violence in the context of drug addiction is due largely to securing the resources to maintain a drug habit as well as to establishing and conducting the business of drug dealing. Neither animal nor human data suggest a direct, pharmacological association between violence and acute or chronic administration of opiates. Although measures of hostility and anger are increased in addicts seeking methadone treatment, these feelings usually do not lead to aggressive or violent acts. Rather, the tendency to commit violent crimes correlates with preaddiction rates of criminal activity. However, experimental studies in animals point to the phase of withdrawal from chronic heroin as the period during which the individual is most vulnerable to being provoked to heightened levels of aggressive behavior. Nevertheless, although humans undergoing opioid withdrawal may experience increased feelings of anger, there is no evidence suggesting that they are more likely to become violent as a result.

PSYCHOMOTOR STIMULANTS

The most serious link of amphetamine to violence occurs in individuals who, after taking intravenous amphetamine—most often chronically—develop a

paranoid psychotic state during which they commit violent acts. Most psychiatric reports and police records do not support the commonly held psychiatric opinion of the early 1970s that amphetamines, more than any other group of drugs, may be related specifically to aggressive behavior. The prevalence of violence by individuals who experience amphetamine paranoid psychosis may be less than 10 percent in general population samples and as high as 67 percent among individuals who showed evidence of psychopathology prior to amphetamine use. Low acute doses of amphetamine can increase various positive and negative social behaviors; higher doses often lead to disorganizing effects on social interactions and to severe social withdrawal. In the early twenty-first century the neurobiological mechanisms for the range of amphetamine effects on aggressive and social behavior remain unknown.

Surprisingly few pharmacological and psychiatric studies exist on cocaine's effects on aggression and violence; the available evidence points to psychopathological individuals who may develop the propensity to engage in violent acts. Cocaine has also been shown to induce a paranoid state, which may heighten the risk of violence. However, the far more significant problem is the violence associated with the supply, dealing, and procurement of cocaine, as documented in epidemiological studies.

HALLUCINOGENS

Most experimental studies with animals and humans, as well as most data from chronic cannabis users, indicate that preparations from the plant (e.g., marijuana and hashish) or the active agent tetrahydrocannabinol (THC) decreases aggressive and violent behavior. Owing to the drug's relatively widespread access, lower cost, and characteristic pattern of use, socioeconomic causes of violence in cannabis dealing and procurement are less prominent than with cocaine or heroin. Novel molecular pharmacological tools will enable a more adequate characterization of the endocannabinoid system in modulating aggressive behavior.

LSD has not been in widespread use since the 1980s, but older data suggest that rarely certain psychopathological individuals while using LSD may engage in violent acts. Phencyclidine (PCP) cannot be causally linked to violent or assaultive behavior in the population as a whole. It appears that personality traits and a history of violent behavior determine whether or not PCP intoxication leads to violence. PCP violence is a relatively rare phenomenon, although when it occurs, the violence stands out because of its highly unusual form and intensity. The risk for such violence depends on the individual's social and personal background.

The impact of genetic predispositions to the susceptibility to become involved with dependence-producing drugs—such as alcohol, heroin, or cocaine—and to act violently has not yet been delineated in terms of specific neural mechanisms. Similarly, the modulating influences of learning, social modeling, or parental physical abuse on the neural substrate for drug action and for aggressive behavior have only recently begun to be specified. Because these critical connections remain incompletely understood, it is not possible at present to identify specific modes of intervention on the basis of neurobiological data.

See also **Alcohol: Psychological Consequences of Chronic Abuse; Crime and Alcohol; Crime and Drugs.**

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AGING, DRUGS, AND ALCOHOL.

Despite the aging of the U.S. population and the resultant increase in the proportion of adults living to an advanced age, relatively little research has examined the correlates, predictors, and consequences of substance use among older adults. Thus, substance misuse in later life—which includes the use of alcohol and illicit, prescription, and over-the-counter drugs—has been called an "invisible epidemic" (Widlitz & Marin, 2002). Although older adults report lower levels of substance use than their younger counterparts, demographic changes and cohort trends suggest that substance misuse in later life is a pressing public health matter, and that older adults represent a group in need of specialized substance treatment programs and services (Gfroerer et al., 2003). Not only are older adults the fastest-growing segment of the U.S. population, but over the first decades of the twenty-first century, the aging population will include the "baby boomers," or individuals born between 1946 and 1964. The aging of the baby boom cohort presents unique challenges to both health and social service sectors, for in addition to reporting higher rates of illicit drug and alcohol use and abuse, the baby boom cohort is significantly larger than previous cohorts (Koenig et al., 1994).

An examination of rates of substance use and misuse among older age groups helps shed light on the potential public health impact of these demographic trends. Although alcohol misuse is often underreported and, accordingly, underestimated in later life, epidemiological work shows that alcohol use and misuse are common among older adults. In 2006, the National Survey on Drug Use and Health (NSDUH) reported that 48 percent of adults aged 60 to 64 had consumed alcohol in the past month. Further, 35.2 percent reported non-binge or non-heavy use, 10.1 percent reported binging behavior (more than 5 drinks at one time on at least 1 day in the past 30 days), and 2.7 percent reported heavy use (over 5 drinks at one time on 5 or more days in the past 30 days) (SAMHSA, 2006). Problematic drinking among the baby boomers was notably higher, however, with 22 percent of adults aged 50 to 54 categorized as heavy or binge drinkers. Adults aged 65 and above reported slightly lower rates of use, with 38.4 percent reporting past-month alcohol use, with 30.8 percent, reporting non-binge or non-heavy use, 6.0 percent reporting binging behavior, and 1.6 percent reporting heavy use. Moreover, epidemiological studies estimate that from the early 1990s until 2002, the prevalence of alcohol abuse or dependence tripled among adults aged 65 and older, with 2.36 percent of older men and 0.38 percent of older women meeting diagnostic criteria for alcohol abuse, and an additional 0.39 percent of older men and 0.13 percent of older women meeting criteria for alcohol dependence (Grant et al., 2004).

In addition, analyses of adults aged 65 and above who completed the 2001–2002 National Survey on Alcohol and Related Conditions (NESARC) yielded 12-month prevalence estimates of 1.5 percent, 1.2 percent, and 0.2 percent for alcohol use disorder, alcohol abuse, and alcohol dependence, respectively (Hasin et al., 2007). Given that substance misuse is more likely to be presented in health care settings, rates of alcohol misuse are often high among primary care (Kirchner et al., 2007), mental health (Holroyd & Duryee, 1997), and nursing home (Oslin et al., 1997) samples. For example, in a 2007 study of older adults in primary care settings, Kirchner et al. reported that of the 24,863 individuals screened, 21.5 percent drank within recommended levels (1–7 drinks per week), 4.1 percent were at-risk drinkers (8–14 drinks per week), and 4.5 percent were heavy (more than 14 drinks per week) or binge drinkers.

Compared to alcohol use, illicit drug use among older adults is relatively rare. For example, data from the Epidemiological Catchment Area (ECA) study imply that in the early 1980s, the lifetime prevalence of drug abuse and dependence was 0.12 percent for older men and 0.06 percent for older women, while the lifetime history of illicit drug use was 2.88 percent and 0.66 percent for men and women, respectively (Anthony & Helzer, 1991). Other work, however, suggests that illicit substance use is more common among older adults than previously estimated (McBride et al., 1992; Schonfeld & Dupree, 2000). Data from the 2001–2002 NESARC, for instance, yielded 12-month prevalence estimates of 0.20 percent for drug use disorder, 0.10 percent for drug abuse, and 0.10 percent for drug dependence (with lifetime prevalence estimates of 0.6%, 0.5%, and 0.2%,

respectively) for adults aged 65 and older (Compton et al., 2007). Drug use among the baby boomers is of particular concern. According to the National Household Survey on Drug Use and Health (NSDUH), the percentage of adults in this age cohort that reported having used illicit drugs in the past month increased from 3.4 percent to 6.0 percent between 2002 and 2006 (SAMHSA, 2006). Thus, rates of illicit drug use and abuse will likely continue to rise as the baby boomers age.

When exploring alcohol and drug use among older populations, it is important to address the use of legal drugs. Given that aging is accompanied by an increased susceptibility to multiple diseases, which may be chronic, acute, infectious, or degenerative in nature, older adults use pharmacological and health services more often than any other segment of the population. For example, older adults are more likely to take multiple medications relative to their younger counterparts, with 71 percent regularly taking at least one prescription medication and 10 percent reporting taking five or more medications (Lassila et al., 1996). Further, it has been estimated that the average older patient takes 5.3 prescription medications each day (Golden et al., 1999). The use of over-the-counter drugs, such as aspirin, diet aids, and decongestants, is also quite common. In one study, 87 percent of older adults reported regular use of over-the-counter medications and 5.7 percent reported the concurrent use of five or more over-the-counter medications (Stoehr et al., 1997). *Polydrug abuse* (also known as *polypharmacy*), or the concurrent use of multiple drugs, is of particular concern in situations where complex medication regimens are not carefully and appropriately adhered to by patients or monitored by physicians. Older adults often see multiple health care providers, and if a clinician is unaware of the medications prescribed by all the other clinicians treating the patient, two or more of these medications may interact, sometimes with fatal results (Monane, Monane & Semla, 1997; Stein, 1994). It is therefore imperative to be cautious when prescribing or recommending a treatment. Both risks and benefits should be taken into account when determining a treatment plan, and guidelines for appropriate use should be clearly communicated to patients.

In light of the high prevalence of pharmaceutical drug use in later life, the risk of misusing prescription and over-the-counter medications increases with age. Although the literature on this topic is sparse, a review of existing work suggests that 11 percent of older women misuse prescription drugs, with projections that 2.7 million adults will be using prescription drugs for nonmedical purposes by the year 2020, (Simoni-Wastila & Yang, 2006). According to Rummans, Evans, Krahn, & Fleming (1995), a large proportion of the medications prescribed to older adults include psychoactive, mood-altering drugs (e.g., drugs for psychosis, depression, anxiety, and sleep problems). For example, the use of benzodiazepines, which are among the most commonly prescribed medications in the United States, increases with age and tends to be chronic in later life (Simon et al., 1996). This is troubling, given that psychotherapeutic medications are subject to improper use and can lead to negative health outcomes, whether used alone or in combination with other drugs or alcohol. Thus, both alcohol and prescription-drug misuse may result in physical, psychological, and social problems and premature death among older adults as a result of factors such as severe withdrawal symptoms, medical complications, and suicide. Furthermore, all these factors taken together—alcohol, old age, multiple diseases, and multiple medications—can lead to poisonous, even fatal, interactions if not closely assessed and monitored. The complexities of age, alcohol, and drug interactions are discussed in the sections that follow.

GUIDELINES AND CLASSES OF SUBSTANCE USE IN LATER LIFE

To properly identify and care for individuals with drug or alcohol problems, it is important to understand both drinking guidelines and the full range of substance use behavior seen among older adults. Due to physiological changes, which are outlined below, guidelines and recommendations for use of these substances by older adults differ from those applied to younger adults. The Treatment Improvement Protocol (TIP) for older adults developed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the Center for Substance Abuse Treatment (CSAT) states that people aged 65 and above should consume no more than one standard drink per day (Blow, 1998; National Institute on Alcohol Abuse and Alcoholism, 1995). In addition, older adults should not consume more than two standard drinks on any one occasion (i.e., binge drinking).

Disulfiram (Antabuse)

Hypoglycemic agents
chlorpropamide (Diabinese)
tolbutamide (Orinase)

Other drugs
cefamandole (Mandole)
cefmetazole (Zefazone)
cefoperazone (Cefobid)
Cefotetan (Cefotan)
chloramphenicol (Chloromycetin)
furazolidone (Furoxone)
griseofulvin (Fulvicin)
ketoconazole (Nizoral)
Metronidazole (Flagyl)
monoamine oxidase inhibitors (e.g., phenelzine and tranylcypromine)
moxalactam (Moxam)
procarbazine (Matulane)
quinacrine (Atabrine)

Alcohol sensitizing mushrooms
Coprinus atramentarius (inky cap mushroom)
Clitocybe clavipes

Table 1. Drugs producing antabuse-like reactions with alcohol. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

There are no set recommendations for prescription and over-the-counter drugs, however, for the appropriate prescription and use of these medicines must be considered on a case-by-case basis. Lastly, there are no safe limits for the use of tobacco, marijuana, or other illicit drugs.

In spite of these recommendations, there is still a great deal of variability in the degree to which older adults use alcohol and drugs. As outlined by Frederic C. Blow (1998), using both the clinical experience and research findings of addiction specialists, a number of categories have been created to capture this variability. Individuals who report drinking less than one to two drinks in the previous year are described as *abstainers.* This is the most common drinking pattern in later life, with approximately 50 percent to 70 percent of older adults reporting abstinence. *Low-risk, social,* or *moderate drinkers* include individuals who drink within the recommended guidelines and do not demonstrate any alcohol-related problems. Individuals with *low-risk medication/drug use* adhere to physicians' prescriptions. It is still important, however, to monitor the number and types of medications being used, as harmful medication interactions may still occur among this group.

Older adults who consume substances above recommended levels (e.g., more than 1 drink/day, high medication doses or durations that exceed reasonable clinical practice), yet experience minimal or no substance-related health, social, or emotional problems represent *at-risk or excessive substance users.* When the use of alcohol or drugs is at a level at which adverse medical, psychological, or social consequences have occurred or are significantly likely to occur, older adults are said to follow a pattern of *problem use*. According to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*), *substance abuse* is a maladaptive pattern of substance use that results in clinically significant impairment or distress (within a 12-month period), as evidenced by difficulty in one or more of the following domains: reduced ability to fulfill common roles (i.e., social, educational, and/or occupational); continued substance use in physically dangerous situations; repeated substance-related legal problems, and continuation of use regardless of substance-related social or interpersonal problems (American Psychiatric Association, 1994). Finally, according to *DSM-IV* criteria, older adults with *alcohol or drug dependence* have a medical disorder marked by clinically significant distress or impairment coupled with preoccupation with alcohol or drugs, loss of control, continued substance use despite adverse consequences, and/or physiological symptoms such as tolerance and withdrawal. Although there has been some debate regarding the validity of *DSM* diagnostic criteria for older adults, identifying older adults with alcohol or drug dependence is essential, as this represents a group in need of specialized treatment and services. Indeed, understanding patterns of use, as a whole, can help inform the proper screening, diagnosis, and counseling of older adults in numerous settings.

CORRELATES AND CONSEQUENCES OF SUBSTANCE MISUSE IN OLDER ADULTHOOD

A great deal of work has focused on identifying factors that are related to increased susceptibility to substance misuse and the maintenance of problematic substance-use patterns in later life. Results suggest that gender, medical comorbidity, a history

of past substance use, and social and family environment represent just a few of these factors. For example, older men tend to drink greater quantities of alcohol than older women, and they are more likely to have alcohol-related problems (Moore et al., 2005) and a longer history of problem drinking (D'Archangelo, 1993). Women who abuse alcohol, however, are more likely than their male counterparts to have been married to a problem drinker, report negative life events and ongoing difficulties with spouses and other family members, and have a history of depression (Brennan & Moos, 1990). Age-related losses in social, physical, and occupational domains (such as widowhood and the death of family and friends); reduced physical function; and retirement also contribute to the adoption or maintenance of abusive drinking patterns in later life among both men and women (Blow, 1998).

Factors such as declining physical health and age-related physiological changes will increase both exposure and reactivity to medications, thus increasing the possibility of misusing these substances in later life. Moreover, women are more likely to use and misuse psychoactive medications (Simoni-Wastila & Yank, 2006), especially if they have a lower socioeconomic status (e.g., lower levels of education and income), are divorced or widowed, or have been diagnosed with a psychiatric disorder (such as depression) or an anxiety disorder. Generally, comorbid psychiatric diagnoses increase the risk for prescription drug abuse and dependence, regardless of gender. Finally, incorrect prescribing practices and inadequate monitoring of drug reactions and patient adherence by health care providers also increase the odds of problematic drug use (Montamat & Cusack, 1992).

While there is some evidence that low to moderate alcohol use (i.e., drinking within recommended guidelines), is associated with health benefits among older adults (Djousse et al., 2007; Rimm et al., 1991), it is important to recognize that there is no evidence that initiating drinking reduces health risks. Furthermore, abstinence should be recommended for older adults who present with a history of alcohol or drug abuse, are taking certain medications, or have been diagnosed with certain acute or chronic conditions. For example, patients with liver disease and gastrointestinal ulcers should not drink alcohol. Alcohol should also be avoided by patients with damage to the heart or other muscles (which may be the result of previous heavy drinking).

The negative consequences of problematic substance use span multiple social and health domains. Severe addiction or dependence harms the user physically, mentally, emotionally, and spiritually. Many people with substance dependence die from physical complications, accidents, and suicide. Alcohol and drug abuse causes thousands of premature deaths, and the cost of complications contributes billions of dollars to any large nation's health expenditure. Health care costs for a family with an alcoholic member are typically twice those for other families, and up to half of all emergency room admissions are alcohol related. Alcohol abuse also contributes to the high healthcare costs of elderly beneficiaries of government-supported health programs.

In general, the medical complications of alcohol abuse observed in older individuals are the same as those seen in younger individuals. These complications include liver disease; acute and chronic inflammation of the pancreas; inflammation, bleeding, and diseases of the gastrointestinal tract; an increased risk of infections; and disturbances in metabolism. Furthermore, alcohol is primarily a drug that depresses or deadens the central nervous system (CNS). The toxic effects of alcohol abuse can cause brain tissue to shrink or waste away, unsteadiness and lack of coordination in movement, and damage to nerves throughout the body. Even moderate use can lead to adverse health outcomes. Low to moderate alcohol consumption impairs one's ability to drive, and it may increase the risk of accidents and fatal injuries due to falls, motor vehicle crashes, and suicide (Sorock et al., 2006). Depression, memory problems, liver disease, cardiovascular disease, cognitive changes, and sleep problems have also been linked to moderate alcohol use.

These negative effects of alcohol are particularly exacerbated in later life due to normal physiological changes that accompany aging. For example, older adults tolerate gastrointestinal bleeding and infection less well than do younger persons. Older adults are particularly prone to vitamin deficiencies, malnutrition, anemia, loss of bone mass, diseases of the central and peripheral nervous systems, heart conditions, and cancer. Alcohol-induced degeneration of the CNS is compounded

by the normal loss of nerve cells that occurs with advancing age.

Finally, alcohol use represents one of the leading risk factors for the occurrence of adverse drug reactions, and it is known to interfere with the metabolism of certain medications. As a result it can lessen the effectiveness of routine drug therapy or even create new medical problems. Among older adults, excessive alcohol use together with medications can severely compromise and complicate a well-planned therapeutic program. Thus, even casual use of alcohol may be a problem for older individuals, particularly if they are taking medications that interact with alcohol. Difficulties can also arise from the interaction of alcohol and over-the-counter medications.

AGING AND ALTERED PHYSIOLOGICAL RESPONSE

As previously mentioned, physiological factors render older adults more sensitive to alcohol, illicit drugs, and over-the-counter and prescription medications, so that guidelines and recommendations for use of these substances differ for older and younger adults. Physiological differences stem from age-related changes in pharmacokinetics—the bodily processes that absorb, distribute within the body, make use of, and excrete substances—which affect the levels of alcohol and drugs in blood and tissues (Vestal & Cusack, 1990). For example, with aging, the percentage of water and lean tissue (mainly muscle) in the body decreases, while the percentage of fat tissue increases. These changes affect the distribution of alcohol and drugs to different parts of the body, the length of time that they stay in the body, and the amount of these substances absorbed by body tissues. One reason that drinking the same amount of alcohol has a greater effect on older adults is that there is a smaller volume of total body fluids, resulting in higher blood-alcohol levels than in young persons (Vestal et al., 1977).

Changes in metabolism, kidney function, and the CNS also are responsible for differential age-related physiological responses. Most substances are eliminated from the body by metabolism in the liver followed by excretion by the kidney. Although enzymes continue to metabolize at the same rate in the old as in the young, both the total weight of the liver (as a percentage of total body weight) and the total blood flow through the liver decrease with age (Loi & Vestal, 1988). As a result, the overall capacity of the liver to convert substances into their inactive by-products declines with age. Furthermore, both the rate at which the kidney filters the blood and the total flow of blood through the kidneys decline with age. Substances are thus excreted more slowly in older adults' urine, and hence build up more quickly in the bloodstream. Finally, nerve-cell sensitivity increases with age, causing drugs that act on the CNS to produce a stronger effect in older patients.

Given the physiological changes outlined above, it comes as little surprise that older adults are more susceptible than younger adults to unintended, adverse drug reactions (ADRs). The overall incidence of ADRs in this age group is two to three times that found in young adults. Although the results of studies vary, about 20 percent of all adverse drug reactions occur in elderly persons (Korrapati, Loi, & Vestal, 1992). ADRs are more severe in older individuals than among young adults. For instance, any drug that affects alertness, coordination, and balance will likely cause more falls and other accidents in older persons than in younger ones. Furthermore, hangover effects of sedative-hypnotic drugs and other mind-altering medicines—such as antipsychotics, antidepressants, and anxiolytics—are common and often more serious for older adults. These hangover effects suggest, in part, that the receptors in older adults' nerve cells are more sensitive, and perhaps supersensitive, to the presence of these medicines, though such effects could also be due to the reduced clearance of medications in older adults, as described above.

Adverse effects of medications may be caused or increased by age-related chronic diseases, by intake of alcohol, and/or by incompatibilities between the foods and medicines that are taken. For example, older adults who drink regularly, even if they are not alcoholic, and/or who use illicit drugs place themselves at increased risk for adverse effects. Consuming alcohol in combination with prescription or over-the-counter drugs may lead to exaggerated or negative effects or, conversely, a blunting of the effectiveness of some medications due to alcohol's effects on metabolism (Moore et al., 2007). The combination of alcohol and prescribed or over-the-counter sleeping pills, for

instance, could decrease intellectual function by producing an organic brain syndrome; frequent results include confusion, falls, wild swings in emotions, and other ADRs (Adams, 1995). Finally, there is some evidence to suggest that women and persons living alone, suffering from multiple diseases, taking multiple drugs, with poor nutritional habits, and with decreased sensory perception or mental clarity are at increased risk of ADRs.

ALCOHOL AND DRUG INTERACTIONS AMONG OLDER ADULTS

It is very difficult to determine the actual incidence of combined drug and alcohol use among adults in later life, but it is likely to be reasonably high for the following reasons: (1) the average adult over sixty-five takes from two to seven prescription medicines daily, in addition to over-the-counter medications; (2) most older persons do not view alcohol as a drug, and they therefore falsely assume that modest amounts of alcoholic beverages can do little harm to an already aged body; and (3) few older persons hold to the traditional notion that mixing alcohol and medications will have bad consequences.

The underreporting, underrecognition, and underestimation of alcohol-drug interactions may lead to dangerous and adverse health consequences, particularly because older adults have an increased sensitivity to both alcohol and drugs, due to the physiological changes outlined above. Interactions between alcohol and over-the-counter or prescription medications, which are commonly used by older adults for a variety of acute and chronic medical conditions, may be especially harmful. Among older adults, the consumption of alcohol in combination with prescription or over-the-counter drugs may lead to exaggerated or adverse therapeutic effects, or to a blunting of the effectiveness of some medications (Moore et al., 2007). For example, antihistamines, including diphenhydramine (Benadryl), dimenhydrinate (Dramamine), and most cold medications and anticholinergics, such as scopolamine, can cause confusion in the elderly, which is exacerbated by concurrent alcohol use. Moreover, alcohol consumed in combination with drugs used to treat type II diabetes (e.g., sulfonylureas), a common condition in older adulthood, may cause dangerously low levels of blood sugar, especially in patients whose diet calls for decreased carbohydrates.

- Elderly patients are advised to avoid alcohol consumption just before going to bed in order to avoid sleep disturbances.
- Because of the potential for alcohol–drug interaction, alcohol ingestion should be avoided before driving.
- Abstinence from alcohol by older patients receiving CNS depressants, analgesics, anticoagulants, antidiabetic drugs, and some cardiovascular drugs is recommended.
- A doctor or pharmacist should be consulted about alcohol–drug interactions.
- Any side effect or loss of energy should be immediately reported to the physician.
- Older individuals who want to drink, have no medical contraindications, and take no medications that interact with alcohol may consider one drink a day to be a prudent level of alcohol consumption. Alcohol when taken in moderation may be useful.

Table 2. Guidelines for use of alcohol by older adults. (Adapted from M. C. Dufour, L. Archer, & E. Gordis. (1992). Alcohol and the elderly. *Clinical Geriatric Medicine, 8*(1), 127–141.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Finally, alcohol use has been shown to interfere with older adults' metabolism of prescribed medications such as digoxin and warfarin, drugs for which modest changes in blood levels can transform therapeutic effects into dangerous adverse effects (Hylek et al., 1998; Onder et al., 2002).

Although not every medication reacts dangerously with alcohol, a variety of drugs do so consistently. The most dangerous of these reactions occurs when alcohol is combined with another CNS depressant. Since alcohol itself is a potent CNS depressant, its use with barbiturates, sedative-hypnotics, or other sedating drugs adds to and reinforces their CNS-depressant effects, which further decreases mental alertness, consciousness, and control of movement (Gerbino, 1982). In one study of older adults, diazepam (Valium), codeine, meprobamate (Equanil), and flurazepam (Dalmane) were the top four agents responsible for drug-alcohol interactions (Jinks & Raschko, 1990). The interaction of alcohol with benzodiazepine drugs may be especially harmful among older adults. This is especially true for diazepam (Valium) and chlordiazepoxide (Librium), due to their long duration of effects. Commonly observed side effects of these medications when combined with alcohol include high blood pressure, sleepiness, confusion, and depression of the CNS, which may lead to slowed or stopped breathing. Similarly, excessive or acute alcohol use increases the CNS effects of tricyclic antidepressants, thus increasing the chances of falls, broken bones, and,

in extreme cases, severe drowsiness, lowered body temperature, coma, and death.

CONCLUSION

It is projected that by the year 2020, the number of older adults requiring substance abuse treatment will increase to 4.4 million, a number that far exceeds the estimated 1.7 million that were in need of treatment in 2000 and 2001 (Gfroerer et al., 2003). The capacity of older adults to handle alcohol and drugs differs from that of the young because of age-related changes in various systems of the body. Alcohol abuse among older adults can lead to falls, fractures, and other similar medical complications. The combination of prescription and over-the-counter medications with alcohol consumption can lead to disastrous complications and even premature death. Thus, older adults and their families or caregivers are encouraged to seek the advice of their pharmacist or family physician in regard to mixing alcohol and medications, and to follow the guidelines given in Table 2.

Although substance misuse among older adults represents a pressing public health issue, individuals in need of treatment or at risk for future problems often go unidentified and untreated. To meet the special needs of older adults experiencing problems with alcohol and drugs, it is important that social service and health care professionals learn to recognize age-specific signs and symptoms of substance misuse, and to be informed regarding available treatment options for older adults. The literature on treatment outcomes among older adults, though scant, is promising. Specifically, treatment outcomes for older adults have been shown to be comparable or significantly better than outcomes among younger adults (Lemke & Moos, 2003; Oslin et al., 2002; Satre et al., 2004). Thus, despite popular belief, older adults are amenable and responsive to treatment, particularly when they are in programs that offer age-appropriate care and include providers who are aware of aging issues. Further research and clinical efforts directed towards identifying and reducing problematic substance use will foster improvements in overall quality of life among older adults with substance use problems.

See also **Diagnostic and Statistical Manual (DSM); Drug Interactions and Alcohol; Drug Metabolism; National Survey on Drug Use and Health (NSDUH); Polydrug Abuse; Social Costs of Alcohol and Drug Abuse; U.S. Government Agencies: Center for Substance Abuse Treatment (CSAT); U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA).**

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AGONIST. An agonist is a drug or an endogenous substance that binds to a receptor (it has affinity for the receptor binding site) and produces a biological response (it possesses intrinsic activity). The binding of a drug agonist to the receptor produces an effect that mimics the physiological response observed when an endogenous substance (e.g., hormone, neurotransmitter) binds to the same receptor. In many cases, the biological response is directly related to the concentration of the agonist available to bind to the receptor. As more agonist is added, the number of receptors occupied increases, as does the magnitude of the response. The potency (strength) of the agonist for producing the physiological response (how much drug is needed to produce the effect) is related to the strength of binding (the affinity) for the receptor and to its intrinsic activity. Most drugs bind to more than one receptor; they have multiple receptor interactions.

See also **Agonist-Antagonist (Mixed); Antagonist.**

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AGONIST-ANTAGONIST (MIXED). A mixed agonist-antagonist is a drug or receptor ligand that possesses pharmacological properties similar to both agonists and antagonists for certain receptor sites. Well-known mixed agonist-antagonists are drugs that interact with opioid (morphine-like) receptors. Pentazocine, nalbuphine, butorphanol, and buprenorphine are all mixed agonist-antagonists for opioid receptors. These drugs bind to the μ (mu) opioid receptor to compete with other substances (e.g., morphine) for this binding site; they either block the binding of other drugs to the μ receptor (i.e., competitive antagonists) or produce a much smaller effect than that of "full" agonists (i.e., they are only partial agonists). Therefore, these drugs block the effects of high doses of morphine-like drugs at μ opioid receptors, while producing partial agonist effects at κ (kappa) and/or δ (delta) opioid receptors. Some of the mixed opioid agonist-antagonists probably produce analgesia (pain reduction) and other morphine-like effects in the central nervous system by binding as agonists to κ opioid receptors.

In many cases, however, there is an upper limit (ceiling) to some of the central nervous system effects of these drugs (e.g., respiratory depression). Furthermore, in people physically addicted to morphine-like drugs, the administration of a mixed

opioid agonist-antagonist can produce an abstinence (withdrawal) syndrome by blocking the μ opioid receptor and preventing the effects of any μ agonists (i.e., morphine) that may be in the body. Pretreatment with these drugs can also reduce or prevent the euphoria (high) associated with subsequent morphine use, since the μ opioid receptors are competitively antagonized. Therefore, the mixed opioid agonist-antagonists are believed to have less abuse liability than full or partial opioid receptor agonists.

As more and more subtypes of receptors are discovered in other neurotransmitter systems (there are now more than five serotonin receptor subtypes and five dopamine receptor subtypes), it is quite likely that mixed agonist-antagonist drugs will be identified that act on these receptors as well.

See also **Agonist; Antagonist.**

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AIDS (ACQUIRED IMMUNE DEFICIENCY SYNDROME).

See **Alcohol and AIDS; Injecting Drug Users and HIV; Needle and Syringe Exchanges and HIV/AIDS; Prisons and Jails: Drug Use and HIV/AIDS in; Substance Abuse and AIDS.**

AL-ANON.

Al-Anon is a fellowship very similar to Alcoholics Anonymous (AA), but it is for family members and friends of alcoholics rather than alcoholics themselves. Although formally separate from the fellowship of AA, it has incorporated into its groups the AA Twelve Steps and Twelve Traditions, as well as AA's beliefs and organizational philosophy. These tools and beliefs are directed toward helping families of alcoholics cope with the baffling and disturbing experiences of living in close interaction with an active alcoholic. In this sense, as noted by Rudy (1986), it is a satellite organization of AA.

Proselytizing organizations such as AA, of necessity, attempt to reduce or eliminate the ties of newcomers with other significant persons and groups who are not members. Rather than attempt to sever those bonds for prospective AA members, Al-Anon evolved as a way to include families in a parallel organization, and thus initiate them into the beliefs and practices of AA. In addition, as AA expanded and more alcoholics went into recovery, close relatives became aware that their own personal problems could be reduced by applying AA principles to themselves and working through the Twelve-Step program, even though they were not alcoholic. In 1980 there were 16,500 Al-Anon groups worldwide, including 2,300 Alateen groups of children of alcoholics (Maxwell, 1982).

A BRIEF HISTORY

Early in the 1940s, women married to alcoholic men started attending AA meetings, and they soon began to meet together informally. By the late 1940s there were so many family members at AA affairs that the AA Board of Trustees had to decide how to manage this valuable but perplexing influx. Since relatives of AA members had already begun to hold their own meetings, the board recommended that AA meetings be limited to alcoholics, and that these family groups should be listed at the AA General Service office as a resource for family members of alcoholics. Several spouses of alcoholics began their own clearinghouse committee to coordinate the approximately 90 groups already in existence, and there was soon a separate network distinct from AA. In order to maintain the connection to AA, the founders shortened the first two letters of "alcoholic," and the first four letters of "anonymous" and called the organization Al-Anon, a name that has persisted.

In 1950, Bill W., a founder of AA, persuaded his wife Lois to get involved with the fledgling Al-Anon. The rapidly accumulating lists in the General Service office were turned over to her and to an associate, Anne B., who contacted those on the list, "and soon they had more work than they could handle" (Wing, 1992, p. 136). For two years, the two conducted their activities at Stepping Stones, the suburban home of Bill W. and Lois. In 1952,

they moved to New York City, where volunteer workers could more easily be recruited.

AL-ANON MEMBERSHIP AND MEETING CHARACTERISTICS

The 2006 Al-Anon/Alateen Member Survey indicated that a majority of members are Caucasian (88%), married (57%), and female (85%). In 2008 there were 24,000 Al-Anon Family Groups worldwide, with a majority of these groups in the United States. Using estimates provided by Cermak (1989) on the average size of Al-Anon meetings (which range from 12 to 15 participants), it is estimated that roughly 324,000 people attend Al-Anon each week. According to the 2006 survey, the average age of Al-Anon members is 55, and about 53 percent of members are retired or hold professional or managerial positions. About 59 percent of Al-Anon members have been, or continue to be, married to an alcoholic. Al-Anon members tend, as a rule, to be relatively well educated. About 24 percent of the membership reported having completed some college, 26 percent reported having earned a college degree, and 24 percent reported having completed some postgraduate education. In general, 30 percent of Al-Anon members are relatively new to Al-Anon (less than 2 years as members), although about one in four members (23%) report long-term affiliation (over 20 years). Typically, Al-Anon members attend five to seven meetings each month, and approximately 59 percent of Al-Anon members have a sponsor or a mentor who aids a member through the prescribed twelve steps of Al-Anon.

AL-ANON'S STRATEGY

Al-Anon strives to direct its members' attention away from the active alcoholic with whom they attempt to interrelate, and toward their own behavior and emotions. This strategy is based on the impression that, in many ways, the family members of alcoholics have personalities that resemble those of alcoholics. That is, they repeatedly attempt to control the feelings and behaviors of the alcoholics in their midst by simple force of personal will, much as alcoholics attempt to control their drinking by the sheer force of their individual will. In both instances, a denial syndrome emerges that protects their compulsive drive toward continued control. In sum, family members often become codependent, so that they become as obsessed with the alcoholic's behavior as he or she is with the bottle (Huppert, 1976).

For example, an alcoholic's spouse or partner may often vainly attempt to control the alcoholic's drinking. Except for brief periods, however, most pleas are rejected and most promises are not kept. In such a case, while the alcoholic continues to drink and enjoy the brief emotional payoffs of intoxication, the spouse or other caretaker must try to cope for both of them by running the household, rearing the children, and working steadily to earn a living. If the alcoholic then shows signs of improvement in a treatment center, the spouse or life partner may resent it deeply, for strangers have done more in a short period than all the partner's efforts over the years. It thus appears to the alcoholic's partner and relatives as though they have not been wise enough, or determined enough, or superhuman enough to get the alcoholic in their life to stop drinking.

Al-Anon attempts to introduce the Twelve Steps of AA into the lives of family members in order to reduce the resentments and controlling behavior they typically display. Al-Anon emphasizes an adaptation of AA's first step: "We admit we are powerless to control an alcoholic relative, that we are not self-sufficient." Such a step is an admission that it is a waste of time to try to control what is beyond their capacities. Using this strategy, it is no longer necessary for the family members to deny that their control efforts are powerless, and this relieves them of the enormous sense of accumulated burden and guilt. In addition, it allows acceptance of outside treatment and its possible success.

RESEARCH ON AL-ANON

Only a few studies have investigated the effectiveness of Al-Anon, and nearly all of these studies have done so in the context of randomized clinical trials intended to both help the significant other of a substance abuser and to engage the substance abuser in formal treatment. Barber and Gilbertson (1996), for example, randomized concerned significant others (CSOs) into one of three interventions, and a fourth group of CSOs were referred to Al-Anon. CSOs assigned to individual counseling and Al-Anon reported significant gains in

personal functioning, but—unlike in the formal interventions—none of the affected family members of the CSOs in the Al-Anon group entered substance abuse treatment. In a similar study, Miller and colleagues (1999) reported that the frequency of Al-Anon meeting attendance could be significantly increased when CSOs were assigned to an individualized Al-Anon facilitation therapy relative to interventions with a cognitive behavioral or intervention focus. Significant gains in CSO personal functioning—including reduced depression, increased relationship happiness, and reduced state-trait anger—were reported in all conditions including the Al-Anon group. However, similar to the findings by Barber and Gilbertson (1996), rates of treatment engagement for the substance abusers were lowest in the Al-Anon facilitation group. Thus, consistent with the expressed strategy of the Al-Anon program, evidence suggests that psychosocial improvement may occur over time for Al-Anon participants. Problem drinkers and illicit drug abusers appear to derive less benefit when CSOs become actively engaged in Al-Anon, relative to other interventions for CSOs.

See also **Adult Children of Alcoholics (ACOA); Codependence; Families and Drug Use; Treatment, Behavioral Approaches to: Twelve-Step and Disease Model Approaches.**

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ALATEEN. Alateen is a division of the Al-Anon Family Group. Its members typically are teenagers whose lives have been impacted by someone else's problem drinking. Roughly, 59 percent are age 14 or younger, while 26 percent are ages 15 to 16 and 15 percent are age 17 or more. The problem drinkers in their lives are predominantly one or both parents, but brothers and sisters are not uncommon.

The prevailing story about the origin of Alateen is quite straightforward. Legend has it that in 1957 a 17-year-old in California was attending Alcoholics Anonymous (AA) and Al-Anon meetings with his parents. His father had just gotten sober in AA and his mother was an active member of Al-Anon. Although the teenager decided that the Twelve Steps of AA were helping him, his mother suggested that instead of attending AA meetings he start a teenaged group and pattern it after Al-Anon. The young man found five other teenaged children of alcoholic parents and, while the adult groups met upstairs, he got them together downstairs.

As other teenagers came forward from Al-Anon groups, the idea spread and it is estimated that as of 2008 about 3,500 Alateen groups meet worldwide. In formal terms, however, these groups are an important and an integral part of Al-Anon Family Groups. They are coordinated from the Al-Anon Family Group Headquarters in New York City and tied closely to their public-information programs. Thus, Alateen uses AA's Twelve Steps, but alters step twelve to simply read "carry the message to others," rather than "to other alcoholics." Alateen groups meet in churches and schoolrooms, often in the same building as Al-Anon, but in a different room.

Although there are a few exceptions, an active, adult member of Al-Anon usually serves as a sponsor. Also, members of Alateen can choose a

personal sponsor from other Alateen members or from Al-Anon members.

Alateen enables its members to openly share their experiences and to devise ways of coping with the problem of living closely with a relative who has a drinking problem. The strategy is to change their own thinking about the problem-drinking relative. Alateen teaches that alcoholism is like diabetes—it cannot be cured, but it can be arrested. Members learn that they did not cause it, and they cannot control it or cure it. Scolding, tears, or persuasion, for example, are useless. Rather, "they learn to take care of themselves whether the alcoholic stops or not" (Al-Anon Family Groups, 1991). They apply the Twelve Steps to themselves—to combat their often obsessive thinking about controlling alcoholic relatives and to help them stop denying those relatives' alcoholism. In addition, they adapt and apply AA's Twelve Traditions to the conduct of their groups. For example, they practice anonymity, defining it not as secrecy, but as privacy and the lowering of competitiveness among members. A 1990 survey of Alateen members indicated an increase in the number of black, Hispanic, and other minority members.

In essence, Alateen uses the strategy of AA itself to learn how to deal with obsession, anger, feelings of guilt, and denials. Newcomers, like newcomers in AA, gain hope when they bond with other teenagers to help one another cope with alcoholic parents and other relatives with drinking problems (Al-Anon Family Groups, 2003).

See also **Adult Children of Alcoholics (ACOA); Codependence; Families and Drug Use; Treatment, Behavioral Approaches to: Twelve-Step and Disease Model Approaches.**

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ALCOHOL

This entry includes the following essays:

CHEMISTRY AND PHARMACOLOGY

Alcohol is produced by a chemical process known as fermentation, in which microorganisms (bacteria or yeast) transform the sugars found naturally in fruits, vegetables, and grains into alcohol, carbon dioxide, and energy. Alcohol production can be expedited by providing optimal environmental conditions for these microbes. Five basic molecular forms of alcohol have been discovered. These forms vary only in the number of carbon atoms in each molecule, but this small difference results in substantial differences in their characteristics. Methanol (CH_3OH), for example, is an extremely dangerous form of alcohol that can cause death shortly after ingestion.

The form of alcohol produced intentionally for oral consumption is ethyl alcohol, also called ethanol. Ethanol has a very simple molecular structure: It is composed of only two carbon atoms, six hydrogen atoms, and one oxygen atom (C_2H_5OH). Ethanol is said to be hydrophilic (water-loving) because its chemical structure is similar to water, and the two compounds readily mix together. In addition, both ethanol and water are polar; that is, each molecule has a positive charge on one end and a negative charge on the other end. The polar structures of both alcohol and water cause the molecules to arrange themselves head to tail, with the positive end of one molecule attracting the negative end of another molecule. This is an important property, for it underlies their ability to be mixed together, and ethanol is not consumed in its pure form, but is generally diluted to some degree.

Most drinks with alcoholic content do not exceed an 8 percent concentration (beer is a good example). Wines do not usually exceed 15 percent, and most liquors are still below 50 percent, or 100 proof by weight or volume. The hydrophilic nature of ethanol also allows it to be readily absorbed

following ingestion. Ethanol is not an especially potent compound compared to other drugs of abuse, but because it can be easily consumed in large quantities and is readily absorbed, pharmacologically active blood levels can be reached quickly.

EFFECTS ON THE BODY AND THERAPEUTIC USES

Ethanol is a general central nervous system depressant, producing sedation and even sleep as the dose increases. The degree of this depression is proportional to its concentration in the blood, although this relationship is more predictable when ethanol levels are rising than it is three or four hours later, when blood levels are falling. This variance occurs because during the first 15 or 20 minutes after an ethanol dose, the peripheral venous blood is losing ethanol to the tissues, while the brain has reached equilibrium with the arterial blood supply. Thus, brain alcohol levels are initially higher than venous blood alcohol levels, but since all blood samples for ethanol determinations are taken from a peripheral vein, the venous blood ethanol concentrations are appreciably lower immediately after ingestion than they are a few hours later, when the entire system has achieved equilibrium.

The reticular activating system of the brain stem is the area most sensitive to ethanol's effects, which accounts for the loss of integrative control of the brain's higher functions. Anecdotal reports of a stimulating effect, especially at low doses, are likely due to the depression of the mechanisms that normally control speech and other behaviors that evolved from training or prior experiences. However, there may be a genetic basis for this initial stimulating effect, since rodents that differ genetically show differences in the degree of initial stimulation or excitement. Upon drinking a moderate amount of ethanol, humans may quickly pass through the "stimulating" phase. Memory, the ability to concentrate, and insight are affected next, whereas confidence often increases as moods swing from one extreme to another. If the dose is increased, neuromuscular coordination becomes impaired. It is at this point that drinkers may be the most dangerous, because they are still able to move about but their reaction times and judgment are impaired and sleepiness must be fought. The ability to drive an automobile or operate machinery is therefore compromised. With higher doses, general (sleep) or surgical (unconsciousness) anesthesia may develop, with respiration dangerously depressed.

Ethanol is believed by many to have a number of medicinal, or therapeutic, uses—most of which are based on anecdotal reports, and few have substantiated claims. One well-known but misguided use of ethanol is to treat hypothermia (exposure to freezing conditions). Ethanol dilates blood vessels, bringing warmth from the core of the body to the skin. Although this initial effect of the alcoholic beverage appears to "warm" the patient, essential body heat is actually lost, causing a dangerous drop in core temperature. Another example is ethanol's effects on sleep. It is believed that a "nightcap" relaxes one and puts one to sleep. Indeed, acute administration of ethanol may decrease sleep latency (the time it takes to fall asleep), but this effect dissipates after a few nights. In addition, waking time during the latter part of the night is increased, and there is a pronounced rebound insomnia that occurs once the ethanol use is discontinued.

Some beneficial uses of ethanol have been identified. For pregnant women, ethanol reduces uterine contractions and is used as an emergency treatment to delay premature delivery. It also is used to treat poisoning from methanol and ethylene glycol. Most of ethanol's therapeutic benefits are derived from applying it to the skin, since it is an excellent skin disinfectant. Ethanol can lessen the severity of dermatitis, reduce sweating, cool the skin during a fever, and, when added to ointments, help other drugs penetrate the skin. These therapeutic uses are for acute problems only. Until recently, it was felt that the chronic drinking of ethanol led only to organ damage. Evidence now suggests that low or moderate intake of ethanol (1–2 drinks per day) can indirectly reduce the risk of a heart attack. However, the doses must be low enough to avoid liver or other organ damage. This beneficial effect is thought to be due to the elevation of high-density lipoprotein cholesterol (HDL-C) in the blood, which, in turn, slows the development of arteriosclerosis and, presumably, a heart attack. This relationship has not been proven but has been culled from the results of several epidemiological studies.

Several mechanisms have been proposed to explain how oral ethanol exerts its effects. Originally,

the effects of alcohol were thought to be nonspecific; that is, it was believed that alcohol generally altered the fluidity of cell membranes (particularly neurons). This disturbance alters ion channels in the membrane, resulting in a reduction in the propagation of neuronal transmission. The anesthetic gases share this property with ethanol. Furthermore, it has been shown that the degree of membrane disordering is directly proportional to the drug's lipid solubility. It has also been argued that such membrane effects occur only at very high doses. Scientists now increasingly believe that the effects of alcohol are more specific—that ethanol binds with and alters the function of a group of proteins called ligand-gated ion channels (LGICs). Specifically, ethanol has been found to augment the activity of the neurotransmitter gamma-aminobutyric acid (GABA) by its actions on an LGIC receptor site close to the GABA receptor. The effect of this action is to increase the movement of chloride across biological membranes. Again, this effect would alter the degree to which neuronal transmission is maintained.

Other LGIC neurotransmitter receptors that have been shown to be modulated by ethanol include those that bind glutamate (the NMDA type), glycine, acetylcholine (the nicotinic type), and serotonin (the 5-HT_3 type). Interestingly, some of these receptors are triggered by ethanol while others are inhibited by it, suggesting that the influence is likely nonspecific. Other pathways susceptible to ethanol involve the voltage-dependent calcium channels. These pathways play a major role in neurotransmitter release, hormone secretion, and the regulation of gene expression.

PHARMACOKINETICS AND DISTRIBUTION

Ethanol is quickly and rapidly absorbed, with 20 percent absorbed from the stomach and the rest from the first section of the small intestines (called the duodenum). Thus, the onset of action is related in part to how fast it passes through the stomach. Having food in the stomach can slow absorption because the stomach does not empty its contents into the small intestines when it is full. However, drinking on an empty stomach leads to almost instant intoxication because the ethanol not absorbed in the stomach passes directly to the small intestine. Maximal blood levels are achieved about 30–90 minutes after ingestion. As mentioned earlier, ethanol mixes with water quite well, and once it enters the body it travels to all fluids and tissues, including the placenta in a pregnant woman. After the 20 to 30 minutes required for equilibration, blood alcohol levels are a good estimate of brain alcohol levels. Ethanol freely enters all blood vessels, including those in the small air sacs of the lungs. Once in the lungs, ethanol exchanges freely with the air, making a breath sample a good estimate of the amount of ethanol in the body. A breathalyzer device is often used by police officers to detect the presence of ethanol in an individual.

Between 90 and 98 percent of the ethanol dose is metabolized. The amount of ethanol that can be metabolized per unit of time is roughly proportional to the individual's body weight (and probably the weight of the liver). Adults can metabolize about 120 milligrams per kilogram per hour, which translates to about 30 milliliters (one ounce) of pure ethanol in about three hours. Women generally achieve higher blood alcohol concentrations than men, even after the same unit dose of ethanol per weight, because women have a lower percentage of total body water, and because they may have less activity of alcohol-metabolizing enzymes in the wall of the stomach. The enzymes responsible for ethanol and acetaldehyde metabolism—alcohol dehydrogenase and aldehyde dehydrogenase, respectively—are under genetic control. Genetic differences in the activity of these enzymes account for the fact that different racial groups metabolize ethanol and acetaldehyde at different rates. The best-known example is that certain Asian groups have a less active variant of the aldehyde dehydrogenase enzyme. Thus, when they consume alcohol, they accumulate higher levels of acetaldehyde than other groups, such as Caucasians, which causes a characteristic response called "flushing." This is actually a type of hot flash, with reddening of the face and neck. Some experts believe that the relatively low levels of alcoholism in such Asian groups may be due to this genetically based aversive effect.

TOXIC EFFECTS

Chronic consumption of excessive amounts of ethanol can lead to a number of neurological disorders, including altered brain size, permanent memory loss, sleep disturbances, seizures, and psychoses. Some of these neuropsychiatric syndromes, such as Wernicke's encephalopathy, which causes permanent brain damage, and Korsakoff's psychosis, a

neurologic syndrome resulting from this brain damage, can be debilitating. Other, less obvious, problems also occur during chronic ethanol consumption. The chronic drinker usually fails to meet basic nutritional needs and is often deficient in a number of essential vitamins, which can lead to brain and nerve damage. Chronic drinking also causes damage to a number of major organs.

By far, one of the most important causes of death in alcoholics (other than by accidents) is liver damage. The liver is the organ that metabolizes ingested and body toxins, and it is essential for natural detoxification. Alcohol damage to the liver ranges from acute fatty liver to hepatitis, necrosis, and cirrhosis. Single doses of ethanol can deposit droplets of lipids, or fat, in the liver cells (called hepatocytes). With an accumulation of such lipids, the liver's ability to metabolize other body toxins is reduced. A weekend drinking binge can produce measurable increases in liver fat. In fact, liver fats can double after only two days of drinking even when blood ethanol levels range between twenty and eighty milligrams per deciliter (mg/dL), suggesting that one need not be drunk to experience liver damage.

Alcohol-induced hepatitis is an inflammatory condition of the liver. The symptoms are anorexia, fever, and jaundice. The size of the liver increases, and its ability to cleanse the blood of other toxins is reduced. Cirrhosis is the terminal and most dangerous type of liver damage. Cirrhosis occurs after many years of intermittent bouts with hepatitis or other liver damage, resulting in the death of liver cells and the formation of scar tissue in their place. Fibrosis of the blood vessels leading to the liver can result in elevated blood pressure in the veins around the esophagus, which may rupture and cause massive bleeding. Ultimately, the cirrhotic liver fails to function and is a major cause of death among alcoholics. Although only a small percentage of drinkers develop cirrhosis, it appears that a continuous drinking pattern results in greater risk than does intermittent drinking, and an immunological factor may be involved.

The role of poor nutrition in the development of some of these disorders is well recognized but not very well understood. Ethanol provides 7.1 kilocalories of energy per gram. Thus, a pint of whiskey provides around 1,300 kilocalories, a substantial amount of raw energy that is devoid of any essential nutrients. Even when food intake is high, nutritional disturbances can exist, because ethanol can impair the absorption of vitamins B_1 , B_{12}, and folic acid. Ethanol-related nutritional problems are also associated with magnesium, zinc, and copper deficiencies. A chronic state of malnutrition can produce symptoms that are indistinguishable from chronic ethanol abuse.

Fetal alcohol syndrome (FAS) was recognized and described in the 1980s. Children of chronic drinkers are born deformed, and the abnormality is characterized by reduced brain function—as evidenced by a low intelligence, smaller than usual brain size, slower than normal growth rates, characteristic facial abnormalities (widely spaced eyes and flattened nasal area), other minor malformations, and developmental and behavioral problems. Fetal malnutrition caused by ethanol-induced damage to the placenta can also occur, and fetal immune function appears to be weakened, resulting in the child's greater susceptibility to infectious disease. Depending on the population studied, the rate of FAS ranges from 1 in 300 to 1 in 2,000 live births; however, the incidence is 1 in 3 infants born to alcoholic mothers. A safe lower limit of ethanol consumption for pregnant women that avoids the risk of having a child with FAS has not been established. The lowest reported level of ethanol that resulted in FAS was about 75 ml (2.5 oz.) per day during pregnancy. Among alcoholic mothers, if drinking during pregnancy is reduced, then the severity of the resulting syndrome is reduced.

TOLERANCE, DEPENDENCE, AND ABUSE

Tolerance, a feature of many different drugs, develops rather quickly to many of ethanol's effects after frequent exposure. When tolerance develops, the dose must be increased to achieve the original effect. Ethanol is subject to two types of tolerance: tissue (or functional) tolerance and metabolic (or dispositional) tolerance. Metabolic tolerance is due to alterations in the body's capacity to metabolize ethanol, which is achieved primarily by a greater activity of enzymes in the liver. Metabolic tolerance only accounts for 30 to 50 percent of the total response to alcohol in experimental conditions. Tissue tolerance, however, decreases the brain's sensitivity to ethanol and may be quite extensive. The development of tolerance can take just a few

weeks, or it may take years, depending on the amount and pattern of ethanol intake. As with other central nervous system depressants, when the dose of ethanol is increased to achieve the desired effects (e.g., sleep), the margin of safety actually decreases, as the dose comes closer to producing toxicity and the brain's control of breathing becomes depressed.

Like tolerance, dependence on ethanol can develop after only a few weeks of consistent intake. The degree of dependence can be assessed only by measuring the severity of the withdrawal signs and symptoms observed when ethanol intake is terminated. Victor and Adams (1953) provided perhaps one of the best descriptions of the clinical aspects of ethanol dependence. Patients typically arrive at the hospital with the "shakes," sometimes so severe that they cannot perform simple tasks without assistance. During the next 24 hours, an alcoholic might experience hallucinations, which typically are not too distressing. Convulsions, however, which resemble those in people with epilepsy, may occur in susceptible individuals about a day after the last drink. Convulsions usually occur only in those who have been drinking extremely large amounts of ethanol. If the convulsions are severe and unattended to medically, the individual may die. Many somatic effects, such as nausea, vomiting, diarrhea, fever, and profuse sweating are also part of alcohol withdrawal. Some 60 to 84 hours after the last dose, there may be confusion and disorientation, and more vivid hallucinations may begin to appear. This phase of withdrawal is often called the delirium tremens, or DTs. Before the days of effective treatment, a mortality rate of 5 to 15 percent was common among alcoholics whose withdrawal was severe enough to cause DTs. The presence of other medical problems, which is commonly the case among alcohol-dependent individuals, has been shown to increase the risk of death during delirium tremens.

TREATMENT FOR ALCOHOL DEPENDENCE

The first step in treating alcoholics is to remove the ethanol from the system, a process called detoxification. Since rapid termination of ethanol (or any other central nervous system depressant) can be life threatening, people who have been using high doses should be slowly weaned from the ethanol by taking a less toxic substitute depressant. Ethanol itself cannot be used safely because it is eliminated from the body too rapidly, making it difficult to control the treatment. Although barbiturates were once employed in this capacity, the safer benzodiazepines have become the drugs of choice. Not only do they prevent the development of potentially fatal convulsions, but they reduce anxiety and help promote sleep during the withdrawal phase. New medications are constantly tested for their ability to aid in the treatment of alcohol withdrawal. Once a person has become abstinent, various methods can be used to maintain abstinence and encourage sobriety. Some of these are pharmacologic and others involve social support networks or formal psychological therapies.

One pharmacologic therapy involves making drinking an adverse toxic event for the individual. This is done by giving a drug such as disulfiram (Antabuse) or citrated calcium carbimide, which inhibit the metabolism of acetaldehyde (a toxic by-product of alcohol metabolism). When ethanol is ingested by someone on disulfiram, the acetaldehyde levels rise very high and very quickly. Increased acetaldehyde concentrations result in facial flushing, nausea, and rapid heartbeat; in rare cases, severe reactions have resulted in death due to cardiovascular collapse. Disulfiram has not been successful in maintaining abstinence in all patients, however, and it may be most effective if its daily ingestion is supervised by someone other than the patient (e.g., a spouse).

Another drug, naltrexone (Revia, Vivitrol), an opiate antagonist first introduced for the treatment of opiate dependence, is also used for the treatment of alcohol dependence. Naltrexone has a high affinity for the μ-opiate receptor, part of a reward pathway that has been implicated in the development of alcohol dependence. The exact mechanism by which naltrexone reduces craving for alcohol is not known, but studies suggest that naltrexone blocks natural opiates released by alcohol, making alcohol consumption less rewarding. The precise mechanism of action of another medication used to maintain abstinence, acamprosate (Campral), is not completely understood. The drug is believed to work on the GABA and glutamate systems. Research suggests that chronic alcohol abuse may disturb the balance in the brain between glutamate-mediated excitation and GABA-mediated inhibition, and that acamprosate may help to restore the normal balance.

Many support groups are available to help people remain abstinent. Alcoholics Anonymous (AA) is one of the most widely known and available. The AA program is structured around a self-help philosophy and emphasizes total avoidance of alcohol and any dependence-producing medications. Instead it relies on a "sponsor" system, providing support partners who are personally experienced with alcoholism and alcoholism recovery. A number of other types of psychological and behavioral approaches to treatment are also widely used.

See also **Accidents and Injuries from Alcohol; Alcoholics Anonymous (AA); Alcoholism: Origin of the Term; Blood Alcohol Concentration; Blood Alcohol Concentration, Measures of; Breathalyzer; Complications; Delirium Tremens (DTs); Driving, Alcohol, and Drugs; Driving Under the Influence (DUI); Epidemiology of Alcohol Use Disorders; Fetal Alcohol Syndrome; Gamma-Aminobutyric Acid (GABA); Naltrexone; Social Costs of Alcohol and Drug Abuse; Treatment, Pharmacological Approaches to: Disulfiram; Treatment, Pharmacological Approaches to: Naltrexone; Withdrawal: Alcohol; Withdrawal: Benzodiazepines.**

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HISTORY OF DRINKING (INTERNATIONAL)

Anthropologists view myth as the belief system of a given people or culture. Regarding the first human consumption of alcohol, they may not be able to know for certain, but they conjecture that it may have occurred when individuals tasted overripe fruit or soured grain. The taste, or the feeling that resulted, or both, may have been pleasant enough to prompt repetition and then experimentation. This experience would have occurred various times and at a number of different places.

Alcohol is significant historically. This simple substance, presumably present since bacteria first consumed some plant cells nearly 1.5 billion years ago, became so deeply embedded in human societies that it affected their religion, economics, politics, and innumerable social and ritual activities. Alcohol played different roles from one culture to the next but even within a given culture over time. This single chemical compound, used (or sometimes emphatically avoided), shaped a diverse array of customs, attitudes, beliefs, values, and effects. A brief review of the history of this relationship illustrates both unity and diversity in the ways people have thought about and treated alcohol. (Special attention is paid in this entry to the United States.)

THE ORIGIN OF ALCOHOL

Ethanol, the form of alcohol used to produce favorable effects, is created naturally in the fermentation of exposed fruits, vegetables, and grains that have become overripe and through the intervention of people who accelerate the process by controlling the conditions of fermentation. Drinks that produce various favorable effects, as well as alcohol-related problems, are labeled *alcoholic*, and labels (like other definitions) are cultural constructs. Wine is thought of as a basic component of meals in much of France and Italy; beer is considered a basic component of meals in Scandinavia and Germany. Additionally, some fruit juices, candies, and desserts may have high levels of alcohol but are not labeled as alcohol. Thus many cultural beliefs people have about alcohol relate more to their social habits and expectations than to the actual pharmacological or biochemical substance and its effect on the human body.

According to the Bible, one of the first tasks Noah performed after the great flood was to plant a

vineyard (Genesis 9:21). According to the predynastic Egyptians, the great god Osiris taught people to make beer, a substance that served both religious and nutritional purposes for them. Similarly, early Greeks credited the god Dionysus with bringing them wine, which they drank mainly as a form of worship. In Roman times, the god Bacchus was thought to be both the originator of wine and always present within it. It was a goddess, Mayahuel, with 400 breasts, who supposedly taught the Aztecs how to make *pulque* from the sap of the maguey plant, a mild beer still important in the diet of many Indians in Mexico, where it is often referred to as *the milk of our Mother*. In each of these cultures, alcohol was associated with the supernatural.

PREHISTORY AND ARCHEOLOGY

Archeologists have discovered alcoholic residues in pots dating from 3500 BCE, which proves that wine was made from grapes in Mesopotamia (in the area of modern Iran). This discovery makes alcohol use almost as old as farming, and, in fact, beer and bread were first produced at the same place at about the same time and from the same ingredients. Little is known about the gradual process by which people learned to control fermentation, to blend drinks, or to store and ship them in ways that kept them from souring, but the distribution of local styles of wine vessels serves as a guide to the flow of commerce in antiquity.

Early wines and beers were not similar to modern varieties of these beverages, but historically, the distinction existed between the two: wine is and was generally derived from fruits or berries, whereas beers and ales are and were derived from grain or a grain-based bread. Until as recently as AD 1700, both were often relatively dark, dense with sediments, and extremely uneven in quality. Homemade wines tended to have relatively little in the way of vitamins or minerals but could last a long time if adequately sealed. However, homebrewed beers tended to be highly nutritious but to last only a few days before going sour (i.e., before the fermenting sugars and alcohol were depleted and liquid turned to vinegar).

In Egypt between 2700 and 1200 BCE, beer was an important part of the daily diet, and it was buried in royal tombs and offered to the deities. Many frescos and carvings in Egyptian tombs depict brewing and drinking; early papyri include commercial accounts of beer, a father's warning to his student son about the danger of drinking too much, praises to the god who brought beer to earth, and other indications of its importance and known effects. In fact, the earliest written code of laws, from Hammurabi's reign in Babylon around 2000 BCE, devoted considerable attention to the production and sale of beer and wine, including regulations about standard measures, consumer protection, and the responsibilities of servers.

During the rise of Ancient Greece and the Roman Empire (roughly 800 BCE–AD 400), grapes were grown to the north and westward in Europe, and wine was important for medicinal and religious purposes, although it was not yet a commonplace item in the diet of poor people. The much-touted sobriety of the Greeks is presumably based on their custom of diluting wine with water and drinking only after meals, in contrast to neighboring populations who often sought drunkenness through beer as a transcendental state of altered consciousness. Certainly heavy drinking was an integral part of Greek religious orgies that, in commemorating their deities, later came to be called *Dionysiac* (or, in the case of the Romans, *Bacchic*). Notably, Alexander the Great, who came from the area of Macedonia, or north of Greece, was reported to have used alcohol to drunkenness.

Romans saw their alcohol use as relative temperance by contrast to the boisterous heavy drinking of their tribal neighbors in all directions, whom they devalued as the bearded ones, *barbarians*, meaning those who were other than Roman. The geographic spread of Latin-based languages and grape cultivation coincided with the spread of the Roman Empire through Europe and the accompanying diffusion of the Mediterranean diet—rich in carbohydrates and low in fats and protein—with wine as the usual beverage. In striking contrast were non-Latin speakers, who were less reliant on bread and pasta and without olive oil; they drank beers and meads, and presumably drunkenness was more common. Plato considered wine an important adjunct to philosophical discussion, and St. Paul is said to have recommended it as an aid to digestion.

The Hebrews established a new pattern around the time of their return from the Babylonian exile and the construction of the Second Temple (c. 500 BCE). Religious practice in family rituals included periodic sacred drinking of wine, accompanied by a pervasive ethic of temperance, a pattern that persisted into modern times and distinguished religious Jews from their gentile neighbors. Early Christians (many of whom had been Jews) praised the healthful and social benefits of wine while condemning drunkenness. Many biblical references to drinking are favorable, and the Gospel report that Jesus chose wine to symbolize his blood was perpetuated in the rite of the Eucharist, a Christian sacrament.

From the Iron Age in France (c. 600 BCE), distinctive drinking vessels found in tombs strongly suggest that political leadership involved redistribution of goods to one's followers, with wine an important symbol of wealth. Archeologists have learned so much about the style and composition of pots made in any given area that they can often trace routes and times of trade, military expansion, or migrations by noting where fragments of drink containers are found. Although less is known about Africa at that time, the assumption is that mild fermented home brews (such as banana beer) were commonplace, as they were in Latin America. In Asia, most is known about China, where as early as 2000 BCE grain-based beer and wine were used in ceremony, offered to the gods, and included in royal burials. Indigenous peoples in most of North America and Oceania, curiously, appear not to have had alcoholic beverages until contact with white Europeans.

Alcohol in classical times served as a disinfectant and was thought to strengthen the blood, stimulate nursing mothers, and relieve various ills. It was also used as an offering to both gods and ancestral spirits. Obviously, alcohol and its consumption had highly positive meanings for early peoples, as they do in modern times for many non-Western societies.

FROM 1000 TO 1500

The Middle Ages was marked by a rapid spread of both Christianity and Islam. Large-scale political and economic integration spread with them to many areas that had previously seen only local warring factions, and sharp social stratification between nobles and commoners was evident at courts and manors, where food and drink became more elaborate. National groups began to appear, with cultural differences (including preferred drinks and ways of drinking), increasingly noted by travelers, of whom there were growing numbers. Excessive drinking by poor people was often criticized but may well have been limited to festive occasions. With population increases, towns and villages proliferated, and taverns became important social centers, often condemned by the wealthy as subverting religion, political stability, and the family. But for many peasants and craftspeople, the household remained the primary economic unit, with homebrewed beer being a major part of the diet.

During this period, the use of *hops* (dried leaves of the hop plant used to give beer its distinctive bitter taste), which enhanced both the flavor and durability of beer, was introduced. In Italy and France, wine became even more popular, both in the diet and in commerce. Distillation had been known to the Arabs since about 800, but among Europeans, a small group of clergy, physicians, and alchemists monopolized that technology until about 1200, producing spirits as beverages for a limited luxury market and for broader use as a medicine. Gradual overpopulation was halted by the Black Death (a pandemic of bubonic plague), and schisms in the Catholic Church resulted in unrest and political struggles later in this period.

Across northern Africa and much of Asia, populations, among whom drinking and drunkenness had been lavishly and poetically praised as valuable ways of altering consciousness, became temperate and sometimes abstinent, in keeping with the tenets of Islam and the teachings of Buddha and of Confucius. China and India both had episodes of prohibition, but neither country was consistently so. Among Hindus, some castes drank liquor as a sacrament, whereas others scorned it, vivid proof that a culture, in the anthropological sense of a set of beliefs and practices that guide group members, can include various behaviors and views.

As the Middle Ages gave way to the Renaissance, both population and economy expanded throughout most of Europe. Because the Arabs (who had ruled from 711 to 1492) had been expelled from Spain and Portugal, they cut off overland trade routes to Asia; European maritime

exploration therefore resulted in increasing commerce all around the coasts of Africa. The so-called Age of Exploration led to the startling encounter with high civilizations and other tribal peoples who had long occupied the Americas. Alcoholic beverages appear to have been totally unknown north of Mexico, although a vast variety of beers, chichas, pulques, and other fermented brews were important in Mexico as foods, as offerings to the gods and to ancestral spirits, and as shortcuts to religious ecstasy. Throughout sub-Saharan Africa, home-brewed beers were plentiful, nutritious, and symbolically important, as they came to be described in later years.

During the Middle Ages, drinking was commonplace, little different from eating, and drunkenness appears to have been infrequent, tolerated in association with occasional religious festivals, and of little concern in terms of health or social welfare. Alcoholic beverages were thought to be invigorating to humans, appreciated by spirits, and important to sociability.

FROM 1500 TO 1800

Wealth and extravagance were manifest in the rapidly growing cities of Europe, but so were poverty and misery, as class differences became even more exaggerated. The Protestant Reformation, which set out to separate sacred from secular realms of life, seemed to justify an austere morality that included injunctions against celebratory drunkenness. If the body was the vessel of the spirit, which itself was divine, one should not desecrate it with alcohol. Puritans viewed intoxication as a moral offense, although they drank beer as a regular beverage and appreciated liquor for its supposed warming, social, and curative properties.

Public drinking establishments evolved, sometimes as important town-meeting places and sometimes as the workers' equivalent of social clubs, with better heat and lighting than homes, with news and gossip, games and companionship. Coffee, tea, and chocolate were also introduced to Europe at this time, and each became popular enough to be the focus of specialized shops. But each was also suspect for a time, while physicians debated whether they were dangerous to the health; clergy debated their effects on morality; and political and business leaders feared that retail outlets would become breeding places of crime, labor unrest, and civil disobedience. Brandies (*brantwijns*, liquor distilled from wines to be shipped as concentrates) spread among the aristocracy, and champagne was introduced as a luxury wine, as were various cordials and liqueurs. Brewing and winemaking grew from cottage industries to major commercial ventures, incorporating many technical innovations, quality controls, and other changes.

The gin epidemic in mid-eighteenth-century London is sometimes cited as showing how urban crowding, cheap liquor, severe unemployment, and dismal working conditions combined to produce widespread drinking and dissolution, but the vivid engravings by William Hogarth may exaggerate the problem. At the same time, the artist extolled beer as healthful, soothing, and economically sound. In France, even peasants began to drink wine regularly. In 1760, Catherine the Great set up a state monopoly to profit from Russia's prodigious thirst, and Sweden did similarly soon after.

Throughout the islands of the Pacific, local populations reacted differently to the introduction of alcohol, sometimes embracing it enthusiastically and sometimes rejecting it. Eskimos were generally quick to adopt it, as were Australian Aborigines, to the extent that some interpret their heavy drinking as an attempt to escape the stresses of losing their valued traditional ways of life. Detailed information about the patterns of belief and behavior associated with drinking among the diverse populations of Asia and Africa vividly illustrates that alcohol resulted in many kinds of comportment, depending more on sociocultural expectations than any qualities inherent in the substance.

Throughout Latin America and parts of North America, the Spanish and Portuguese conquistadors found that indigenous peoples already had home brews that were important to them for sacred, medicinal, and dietary purposes. The Aztecs of Mexico derived a significant portion of their nutritional intake from pulque but reserved drunkenness as the prerogative of priests and old men. Cultures throughout the rest of the area similarly used *chicha* (beer made from maize, manioc, or other materials). The Yaqui (in the area of modern Arizona) made a wine from cactus as part of their rain ceremony, and specially prepared chicha was

used as a royal gift by the Inca of Peru. Religious and political leaders from the colonial powers were ambivalent about what they perceived as the risks of public drunkenness and the profits to be gained from producing and taxing alcoholic beverages. A series of inconsistent laws and regulations, including sometime prohibition for Indians, were probably short-lived experiments, affected by such factors as local revolts and different opinions among religious orders.

As merchants from various countries competed to gain commercial advantage in trading with the various Native American groups of North America, liquor quickly became an important item. Indeed, the British colonial government recognized the importance of alcohol among American Indians, insuring a steady supply of alcohol when negotiating treaties with the tribes. At the Treaty of Easton, in 1758, alcohol was said to have flowed freely throughout the bargaining process, an effort by colonial negotiators to extract more lands from the Lenape and Shawnee. For many but not all American Indian tribes in the eighteenth and nineteenth centuries, alcohol was a *deadly medicine* introduced by European settlers. As Pequot author William Apess wrote in 1833, "My sufferings were through the white man's measure, for they most certainly brought spirituous liquors first among my people" (Apess, 1992, p. 121).

A common belief is that Native Americans are genetically vulnerable to alcohol, but some tribes (such as Hopi and Zuni) never accepted it, and others drank with moderation. Indeed, a hereditary mechanism responsible for certain tribes' propensity for drink remains elusive. The Seneca in New York State are an interesting case study because they went from having no contact with alcohol through a series of stages, culminating in a religious ban. When brandy first arrived, friends would save it for an unmarried young man, who would drink it ceremoniously to help in his required ritual quest for a vision of the animal that would become his guardian spirit. In later years, drinking became secular; anyone could drink, and boisterous brawling was a frequent outcome. In 1799, when a tribal leader who was already alcoholic had a very different kind of vision, he promptly preached abstention from alcohol, an end to warfare, and devotion to farming, all of which remain important in modern times in the religion that is named after him, Handsome Lake.

Clearly, alcohol plays many roles in the history of any people, and changes in attitudes can be abrupt, illustrating again the importance that social constructions of reality have in relation to alcohol and its uses.

THE NINETEENTH CENTURY

The large-scale commercialization of beer, wine, and distilled liquor spread rapidly in Europe as many businesses and industries became international in scope. Large portions of the European proletariat were no longer tied to the land for subsistence, and new means of transportation facilitated vast migrations. The industrial revolution was not an event but a process, in which, for many people, work became separated from home. The arbitrary pace imposed by wage work contrasted markedly with the seasonal pace of traditional agrarianism.

In Europe, political boundaries were approximately those of the twentieth century; trains and steamships changed the face of trade; and old ideas about social inequality were increasingly challenged. Alcohol lost much of its religious importance as ascetic Protestant groups, and even fervent Catholic priests in Ireland, associated crime, family disruption, unemployment, and a host of other social ills with it, and taxation and other restrictions were broadly imposed. In Russia, the czar ordered prohibition, but only briefly as popular opposition mounted and government revenues plummeted. Those who paid special attention to physical and mental illnesses were quick to link disease with long-term heavy drinking, although liquor remained an important part of medicine for various curative purposes. In Britain, Europe, and Australia a few institutions sprang up late in the nineteenth century to accommodate so-called inebriates, individuals said to suffer from the disease of inebriety. Although there was little consensus about how or why drinking created problems for some people but not for others, heredity, bad company, and iatrogenic (used to describe a symptom of a disease) causes were cited frequently as leading drinkers into dangerous consumption patterns.

THE TWENTIETH CENTURY

While alcohol remained valued and continually used, cultures began to reassess its role as research and experience provided more understanding

about its effects. World War I prompted many countries to enact national austerity programs curbing the alteration of foodstuffs into alcoholic beverages. Absinthe was thought to be so harmful to one's health that it was prohibited in several European countries. Sweden experimented with rationing alcohol, and Iceland banned beer, but not wine or liquor. Furthermore, the Russian czar again attempted to impose prohibition. Due to excessive rates of heavy alcohol consumption and the resulting societal ills, such as violence, Scandinavian countries implemented a variety of regulations, including state monopolies, increased taxation, and restrictions on the location and times of sale. After employing various regulations and statues, these countries turned to large-scale social research in order to understand and influence excessive alcohol consumption.

While several Western countries were expanding their spheres of influence in sub-Saharan Africa, they agreed briefly on a multinational treaty that outlawed the sale of alcoholic beverages there, although they did nothing to curtail production of domestic drinks by various tribal populations. A flurry of scientific analyses of indigenous drinks surprised many by demonstrating their significant nutritional value, and more detailed ethnographic studies showed how important they were in terms of ideology, for vows, communicating with supernatural beings, honoring ancestors, and otherwise building social and symbolic credit—among native societies not only in Africa but also in Latin America and Asia. Closer attention to the social dynamics of drinking and other aspects of culture showed that the impact of contact with Western cultures is not always negative and that for many peoples the role of alcohol remained diverse and vital.

The worldwide economic depression of the 1930s slowed the growth of alcohol consumption; however, the economic boom that followed World War II caused a rapid rise in drinking. Subsequently, some observed a new temperance movement emerging, which placed greater emphasis on total avoidance of alcohol. A phenomenon that grew out of Scandinavian social research, this movement used a public health approach to address the societal issues associated with alcohol, employing such tactics as increased taxes, warning labels for all alcoholic beverages sold, and banning or restricting alcohol advertising. Prevention strategies such as these, which were already employed throughout the United States, grew in popularity throughout Europe and other countries. In addition, the World Health Organization (WHO) of the United Nations called for a 25 percent worldwide reduction of alcohol consumption between 1985 and 2000. Furthermore, the WHO recommended that member countries adopt similar policies. New assumptions about the role of the state in support of public health and social welfare shaped people's expectations about drinking and its outcomes. Mass media and international conglomerates actively engaged in the expansion of markets, especially into developing countries.

GLOBAL CONSUMPTION OF ALCOHOL IN THE EARLY 2000S

The World Health Organization (WHO) estimated that approximately 2 billion people consumed alcohol beverages worldwide (WHO, 2004). However, the consequences associated with alcohol consumption were not equivalent across all nations. For example, drinking was the leading risk factor for disease burden for low-mortality developing countries and is third-largest among developed countries (Rehm & Eschmann, 2002). In comparing the overall alcohol consumption among 189 member states between the years of 1961 and 2001, the WHO documented a general increase in average alcohol consumption from 1961 to 1980 among adults (individuals 15 years of age or older). Afterwards, global alcohol consumption levels decreased slightly and remained stable at approximately 5.1 liters of pure alcohol (including beer, wine, and spirits) per adult capita. Of that total, 1.9 liters was represented by beer consumption, spirits account for 1.7 liters, and wine accounts for 1.3 liters (WHO, 2004).

However, when examining these trends by region, one gets a much clearer representation of global alcohol consumption. Regions included in the WHO analysis are categorized as follows: African region, region of the Americans, South-East Asia region, European region, Eastern Mediterranean region, and Western Pacific region. The population mean of adult per capita alcohol consumption was highest among the European region. Moreover, the European region's average alcohol consumption (approximately 10.5 liters) was four

liters greater than the next highest region, the Americas (approximately 6.5 liters). In general, regions with the highest mean alcohol consumption (European, African, and the Americas) were decreasing, while regions with the lowest consumption (Southeast Asian and Western Pacific) were increasing. However, the Eastern Mediterranean region exhibited a consistently low level of alcohol consumption, which was perhaps due to the Muslim influence prevalent among the majority of the countries included in that region (WHO, 2004).

See also **Advertising and the Alcohol Industry; Chocolate; Coffee; Tea.**

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HISTORY OF DRINKING IN THE UNITED STATES

When the *Arbella* departed England for Boston's shores in 1630, its Puritan voyagers had stowed away three times as much beer as water, plus some 10,000 gallons of wine. Colonial Americans regarded alcohol as the *Good Creature of God* and early settlers, like their European and British forbears, drew a strong distinction between drinking and drunkenness, the latter being the work of the devil. Whether rum distilled from West Indian sugar, home-brewed beer, or imported wines, alcohol was a staple of colonial life. America's first rum distillery opened in 1700 in Boston, and other coastal New England cities followed in short order, opening their own distilleries and pushing the alcohol preferences of the colonials away from beer and cider toward spirits.

In what is now the United States, colonial drinking patterns and those of the young republic generally reflected the alcohol habits of the

countries from which immigrants had come. Beer was a staple of colonial life and the earliest settlers took to brewing a variety of agricultural products. Connecticut governor John Winthrop, Jr. was said to have brewed a fine beer made from Indian corn, whereas Benjamin Franklin developed a spruce beer. Hard cider was also popular, and colonials began to distill applejack from their cider as well. Rum (distilled from West Indies sugar production) became an important item in international trade, following routes dictated by the economic rules of the British Empire. In the infamous Triangle Trade, captive black Africans were shipped to the West Indies for sale as slaves. Many worked on plantations there, producing not only refined sugar, a sweet and valuable new faddish food, but also molasses, much of which was shipped to New England. Distillers there turned it into rum, which was in turn shipped to West Africa, where it could be traded for more slaves.

Geography also played a role in shaping colonial America's drinking habits. Rum was not easy to transport far inland, so as the settlers pushed further west, grain whiskey became increasingly popular. Farmers in the western settlements produced a surplus of grain, and one bushel of corn could yield 3 gallons of liquor, which not only kept longer than the corn, but also was easier to transport. The arrival of the whiskey-drinking Scotch-Irish on the western frontier pushed rum still further from the alcoholic mainstream. The Scotch-Irish brought their distilling skills with them and improved the quality of American grain whiskey.

The American Revolution (1775/6–1783) interrupted the triangular trade, pushing rum to the periphery, as more North Americans shifted to whiskey. After the war, when the first federal excise tax was imposed (on whiskey) in 1790, to help cut the debt of the new United States, producers' anger about a tax increase was expressed in the Whiskey Rebellion of 1794. To quell the uprising, federal troops (militia) were used for the first time.

Although the first temperance reformers may have been Native Americans seeking to end the damage colonials wrought on their people through alcohol, the American temperance movement is generally said to have begun with Benjamin Rush, a noted physician and signer of the Declaration of Independence. Rush's concerns about the health of the young republic led him to publish *An Inquiry into the Effects of Ardent Spirits upon the Human Body and Mind* in 1784. Fearing that the health of his new nation might be jeopardized by intoxicated voters, Rush could not bear the prospect of drunkards shaping the new republic's destiny. Rush could make a strong case, for elections often featured heavy drinking, and the annual per capita consumption of absolute alcohol figured between 4 and 6 gallons (about twice the rate in 2000). Rush was the first to articulate a disease concept of intemperance; he also distinguished between healthful fermented beverages such as beer and cider, and the more potent and dangerous distilled spirits.

DEVELOPMENTS IN THE NINETEENTH CENTURY

Alcohol flowed freely in a variety of contexts within the United States during the first half of the nineteenth century: Neighbors still drank while helping each other—for example, in barn-raising or reciprocal labor exchange during the harvest. But for the urban masses, leisure and a middle class emerged as new phenomena. Drinking, which was increasingly forbidden in the workplace as dangerous or inefficient, gradually became a recreational activity, often timed to mark the transition between the workday and home life. Within American cities, the saloon, with its whiskey, beer, warm cheap meals, and camaraderie, became an urban fixture—one that social reformers would seize on as the nineteenth century wore on. As markets grew, foods became diverse, so that beers and ciders (usually hard) lost their special value as nourishing and energizing. The rugged individualism of the frontier, touted by presidential candidates such as Andrew Jackson and embodied in the image of the lumberjack, the cowboy, and the miner, seemed to encourage drinking as a sign of virility and patriotism. Per capita alcohol consumption rose precipitously between 1790 and 1830, from an average of 5.8 gallons annually to 7.1 gallons in 1810; this per capita level held relatively steady until the 1830s.

A wave of mounting religious concern that has been called the Second Great Awakening swept over the United States early in the 1800s, however, and by 1850 a dozen states had enacted prohibition. Neo-republicans fearful for the fate of the

young nation and Protestant clergy concerned for the moral health of the republic led the campaign. Lyman Beecher, a Yale-educated Calvinist minister and neo-republican, embodied this reform impulse. Beecher led an evangelical life preaching throughout the United States between 1800 and 1850, urging temperance on his congregations as they built what he believed to be a divinely inspired republic where civil and religious liberty held the day. Temperance, however, was not the only reform pressed on the American people during the Second Great Awakening: Peace, abolition, bans on profanity and Sabbath breaking, women's rights, common school education, and humane treatment of the mentally ill were all championed in the era of reform that preceded the Civil War.

Evangelical Protestant clergymen established the American Society for the Promotion of Temperance in 1826. By 1836 this group had changed its name to the American Temperance Society and adopted a platform of total abstinence (rather than the elimination of only distilled beverages). In the early 1840s Americans rallied in the name of temperance, *taking the pledge* for sobriety and lobbying in record numbers to end the licensing of saloons. The Washingtonian Movement, a grassroots total abstinence movement, held parades and public talks, offered new recruits financial help and moral support, and established institutions for inebriates—Washingtonian Homes—that relied on moral suasion to keep their residents on the water wagon. Late antebellum America also witnessed renewed middle-class campaigns for local and state prohibition. The prohibition laws that were enacted, however, were cast aside as the Civil War loomed. In the years leading up to the War Between the States, however, the Good Creature of God became *demon rum*.

In the Reconstruction period, another wave of sentiment against alcohol arose, as large numbers of immigrants (many of them Catholic and hailing from so-called wet cultures) were seen by Protestant Yankees as trouble: competing for jobs, changing the political climate, and challenging old values. Alcohol, drunkenness, and the saloon were linked to poverty, political corruption, prostitution, and workplace inefficiency; in short, degeneration at the societal and individual levels. Frances Willard's Woman's Christian Temperance Union (WCTU) redefined temperance, along with a host of other social purity reforms as a women's issue involving home protection. At the WCTU's prompting, Congress mandated the inclusion of *scientific temperance* education in all high-school physiology textbooks.

At approximately the same time as the WCTU picked up the temperance torch, a group of physicians, clergy, and social reformers established the American Association for the Cure of Inebriates (AACI), to promote a new specialty of medicine that would manage those whose alcohol consumption had run amuck. Members of the AACI established a network of private institutions to treat habitual drunkards, offering restorative medical, moral, and vocational assistance. California, Iowa, Massachusetts, and New York followed suit, establishing state and municipal inebriate asylums. In this age of industrial capitalism, all institutions endeavored to restore the inebriate's breadwinning potential as well as his sobriety. The AACI faded as the drive for national prohibition grew. By 1920 most of the inebriate institutions had closed their doors and chronic drunkenness was again viewed as a primarily moral, political, and legal issue.

Ultimately, the church-based Anti-Saloon League (ASL), founded in 1895 and supported by such industrial magnates as Henry Ford and Pierre du Pont, spearheaded the drive for prohibition. Under Superintendent Wayne Wheeler, the ASL pursued an innovative bipartisan lobbying strategy that secured prohibitory state legislation and, in 1919, ratification of the Eighteenth Amendment, establishing the United States as a dry nation. Anti-German sentiment and a reaction against German American-owned breweries accompanied World War I and assisted in ending the commercial sale of alcohol.

Native American populations, in the meantime, suffered various degrees of displacement, exploitation, and annihilation, sometimes as a result of deliberate national policy and sometimes as a result of local tensions. The stereotype of the drunken Indian became embedded in novels, news accounts, and the public mind, although the image applied to only a small segment of life among several hundred Native populations. Some Native Americans remained abstinent and some returned to abstinence as part of a deliberate espousal of indigenous values—for

example, in the Native American Church, using peyote as a sacrament, or in the sun dance or sweat lodge, using asceticism as a combined religious and intellectually cleansing precept.

From Asia, Africa, and Oceania, explorers, traders, missionaries, and others brought back increasingly detailed descriptions of non-Western drinking practices and their outcomes. It is from such ethnographic reports, often sensationalized, that we can guess about the earlier distribution of native drinks and can recognize new alcoholic beverages as major commodities in the commercial exploitation of populations. Although some of the sacramental associations of traditional beverages were transferred to new ones, the increasing separation of brewing from the home, the expansion of a money-based economy, and the apparent prestige value of Western drinks all tended to diminish the significance of home brews. In African mines, Latin American plantations, and even some U.S. factories prior to Prohibition, liquor became an integral part of the wage system, with workers required to accept alcohol in place of some of their cash earnings. In some societies where drinking had been unknown before Western colonization, the rapid spread of alcohol appears to have been an integral part of a complex process that eroded traditional values and authority

LEGACY OF THE TWENTIETH CENTURY

It has been said that the average person's life in 1900 was more like that of ancestors thousands of years earlier than like that of most people today. The assertion certainly applies to the consumption of liquor. Pasteurization, mass production, commercial canning and bottling, and rapid transport all transformed the public's view of beer and wine in the twentieth century. The spread of ideas about individualism and secular humanism loosened the hold of traditional religions on the moral precepts of large segments of the population. New assumptions about the role of the state in support of public health and social welfare color society's expectations of drinking and its outcomes. Mass media and international conglomerates are actively engaged in the expansion of markets, especially into developing countries.

World War I prompted national austerity programs in many countries that curtailed the diversion of foodstuffs to alcoholic beverages but did not quite reach the full prohibition for which the United States became famous. Often called *the noble experiment*, the Eighteenth Amendment to the Constitution was the first amendment to deal with the workday behavior of people who have no important public roles. It forbade commercial transaction of alcohol but said nothing about drinking or possession. Most authorities agree that, during the early years of Prohibition, there was relatively little production of alcoholic beverages and not much smuggling or home production. It was not long, however, before illegal sources sprang up. Moonshiners distilled liquor illegally, and bootleggers smuggled it within the United States or from abroad. Speakeasies sprang up as clandestine bars or cocktail lounges, and a popular counterculture developed in which drinking was even more fashionable than before. Some entrepreneurs became immensely wealthy and brashly confident and seemed beyond the reach of the law, whether because of superior firepower, corruption, or perhaps both.

With Prohibition, the U.S. government had suffered from the loss of excise taxes on alcohol, which accounted for a large part of the annual federal budget. The stock-market crash, massive unemployment, the crisis in agriculture, and worldwide economic depression aggravated an already difficult situation, and civil disturbances spread throughout the country. Some of the same influential people who had pressed strongest for prohibition reversed their stands, and the Twenty-first Amendment, the first and only repeal to affect the U.S. Constitution, did away with the federal prohibition of alcohol in 1933. Although the national government retained close control over manufacturing and distribution to maximize tax collection, specific regulations about retail sales were left up to the states. An odd patchwork of laws emerged, with many states remaining officially dry, others allowing a local option by counties or towns, some imposing a state monopoly, some requiring that drinks be served with food, and others expressly prohibiting it, some insisting that bars be visible from the street, and others demanding the opposite, and so on. The last state to vote itself wet was Mississippi, in 1966, and many communities remain officially dry in the early twenty-first century. The older federal law prohibiting the sale of alcohol to Native Americans was not repealed until

1953, and many Indian reservations and Alaskan Native communities remain dry by local choice.

The experience of failed prohibition in the United States is famous, but a similar combination of problems involving lawlessness, corruption, and related issues led to repeal, after shorter experiments, in Iceland, Finland, India, Russia, and parts of Canada, demonstrating again that such drastic measures seem not to work except where supported by consensus and religious conviction (e.g., as in Saudi Arabia, Iran, and Ethiopia). It is ironic that some Native American reservations with prohibition have more alcohol-related deaths than those without. A more salutary factor is the growth of culturally sensitive programs for prevention and treatment that are being developed, often by the communities themselves, for Native and other minority populations.

In the mid-twentieth century a number of alcoholics formed a mutual-help group, modeled in part on the earlier Washingtonians and taking inspiration from the Oxford Group, whose core principles included absolute honesty, absolute purity, absolute unselfishness, and absolute love: Alcoholics Anonymous (AA). AA has grown to be an international fellowship of individuals whose primary purpose is to keep from drinking. At about the same time, scientists from a range of disciplines started to study various aspects of alcohol and alcoholism, and society's knowledge has grown rapidly in the decades since. Because of the large constituency of recovering alcoholics, the subject has become politically acceptable, and the disease concept has overcome much of the moral stigma that was formerly associated with alcoholism. Establishment of a National Institute on Alcohol Abuse and Alcoholism in 1970 signaled a major government commitment to the field, and its incorporation among the National Institutes of Health in 1992 indicates that concerns about wellness have largely displaced theological preoccupations.

Consumption of all alcoholic beverages increased gradually in the United States from repeal until the early 1980s, with a marked increase following World War II, although it never reached more than one-third of what is estimated for the corresponding period a century earlier. Around 1980 sales of spirits started dropping and have continued to do so. A few years later, wine sales leveled off and gradually declined until the late 1990s, when they began to climb again, perhaps in association with the finding that red wine confers some cardiovascular benefit. Beer sales also appear to have passed their peak; they continue to slowly decline. In 2005 Americans consumed, on average, 2.24 gallons of absolute alcohol per year, representing a slight increase from the previous few years, but significantly less than a decade ago. These overall reductions occurred despite increased advertising. They took place along with the return of a new clean living movement that emphasizes physical exercise, the consumption of less-processed foods, and concern for health, especially the prevention of chronic diseases of middle age: obesity, diabetes, cardiovascular disease, and cancer. America's baby boomer generation has also hit midlife, and it seems that this large demographic segment is shaping the nation's drinking habits.

Linked with the reduction in drinking, what some observers call a new temperance movement has emerged, in which individuals not only drink less but also call for others to do the same. The decline would be enforced by laws and regulations that increase taxes, index liquor prices to inflation, diminish numbers and hours of sales outlets, require warning labels, ban or restrict advertising, and otherwise reduce the availability of alcohol. Mothers Against Drunk Driving (MADD), founded in 1980; Students Against Driving Drunk (SADD), established in 1981; and campaigns against fetal alcohol syndrome (FAS), fetal alcohol effect (FAE), and domestic violence associated with alcohol consumption have all increased public awareness of the social destruction drinking may cause apart from the harms that can occur to the drinker. Such a harm reduction approach is by no means limited to the United States. Its popularity is growing throughout Europe and among groups elsewhere, even as alcohol consumption continues to rise in Asia and many developing countries.

See also **Prohibition of Alcohol; Temperance Movement; Woman's Christian Temperance Union.**

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PSYCHOLOGICAL CONSEQUENCES OF CHRONIC ABUSE

Chronic alcohol abuse (heavy drinking over a long period) can lead to numerous adverse effects—to direct effects such as impaired attention, increased anxiety, depression, and increased risk-taking behaviors—and to indirect effects such as impaired cognitive abilities, which may be linked to nutritional deficiencies from long-term heavy drinking.

A major difficulty in describing the effects of chronic alcohol abuse is that many factors interact with such consumption, resulting in marked individual variability in the psychological consequences. In addition, defining what constitutes chronic and abusive drinking in relation to resulting behavioral problems is not simply a function of frequency and quantity of alcohol consumption. For some individuals, drinking three to four drinks per day for a few months can result in severe consequences, whereas for others, six drinks per day for years may not have any observable effects. One reason for this variability is related to genetic differences in the effects of alcohol upon individuals. Though not all of the variability can be linked to genetic predispositions, it has been demonstrated that the interactions between individual genetic characteristics and environmental factors are important in determining the effects of chronic alcohol consumption.

Other factors to consider when assessing the effects of chronic drinking are connected to the age and sex of the drinker. In the United States, heavy chronic drinking occurs with the greatest frequency in white men, ages nineteen to twenty-five. For the majority of individuals in this group, heavy drinking declines after age twenty-five to more moderate levels and then decreases to even lower levels after age fifty. As might be expected, the type and extent of psychological consequences depend on the age of the chronic drinker. Research has indicated that younger problem drinkers are more likely to perform poorly in school, have more arrests, and be more emotionally disturbed than older alcoholics. Also, younger drinkers have more traffic accidents, which may result from a combination of their heavy drinking and increased risk-taking behavior. Many of the more serious consequences of chronic alcohol use occur more frequently in older drinkers—individuals in their thirties and forties; these include increased cognitive and mental impairments, divorce, absenteeism from work, and suicide. Chronic drinking in women tends to occur more frequently during the late twenties and continues into the forties, but the onset of alcohol-related problems appears to develop more rapidly in women than in men. In a study of Alcoholics Anonymous members, women experienced serious problems only seven years after beginning heavy drinking, as compared to an average of more than eleven years for men, a phenomenon that has been called *telescoping* of the adverse effects in women.

Black and Hispanic men in the United States tend to show prolonged chronic drinking beyond the white male's reduction period during his late twenties. Thus, for many of the effects of chronic drinking discussed below, age, sex, and duration of drinking are important factors that mediate psychological consequences.

NEGATIVE CONSEQUENCES

In the early 1990s, it was estimated that between 7 and 10 percent of all individuals drinking alcoholic beverages experience some degree of negative consequences as a result of their drinking pattern. Most people believe that chronic excessive drinking results in a variety of behavioral consequences, including poor work/school performance and inappropriate social behavior. These two behavioral criteria are used in most diagnostic protocols aimed at determining if a drinking problem exists. Several surveys have found that heavy chronic drinking does produce a variety of school- and job-related problems. A survey of personnel in the U.S. armed services found that for individuals considered heavy drinkers, 22 percent showed job-performance problems. Health professionals may also show high rates of alcohol problems, with a late 1980s British survey indicating that physicians experience such problems at a rate of 3.8 times that of the general population. A variety of surveys have consistently shown that chronic excessive drinking leads to loss of support by moderate-drinking family and friends.

Among couples in which only one member drinks, the incidence of divorce is estimated to be over 50 percent. Often the interpersonal problems that surround a problem drinker can lead to family violence; a study published in 2001 found that 30 to 40 percent of men and 27 to 34 percent of

women who commit domestic violence were inebriated at the time of the crime. Other survey data indicate that people who drink alcohol frequently are more likely to become involved with others who share their drinking patterns—particularly those who do not express concern about the individual's excessive and altered behavior that results from drinking. The increased association with fellow heavy drinkers as one's main social-support network can itself result in increased alcohol use.

The interaction between the social setting and the individual, the current level of alcohol intoxication, and past drinking history all play a role in the psychological consequences of chronic heavy drinking. It is impossible to determine which changes in behavior result only from the use of alcohol.

Depression. One major psychological consequence resulting from chronic heavy drinking for a subpopulation of alcohol abusers (predominantly women) is the feeling of loss of control over one's life, commonly manifested as depression. (While not conclusive, some studies suggest that the menstrual cycle may be an additional factor for this population.) In many cases, increased drinking occurs as the depression becomes more intense. It has been postulated that increased drinking is an attempt to alleviate depression.

Unfortunately, since this so-called cure usually has little success, a vicious drinking cycle ensues. While no specific causality can be assumed, research on suicide has indicated that chronic alcohol abuse is involved in 20 to 36 percent of reported cases. The level of suicide in depressed individuals with no alcohol abuse is substantially lower—about 10 percent. It is not clear if the chronic drinking results in depression or if the depression is a preexisting psychopathology, which is exacerbated by the drinking behavior. The rapid improvement of depressive symptoms seen in the majority of alcoholics within a few weeks of detoxification (withdrawal) suggests that, for many, depressive symptoms are reflective of toxic effects of alcohol. In one study, for example, 67 percent of patients acutely hospitalized for alcohol dependence were found to have high levels of depressive symptoms. Following detoxification from alcohol, only 13 percent continued to be depressed. Regardless of the cause, it appears that the combination of depression and drinking can be a potent determinant for increasing the potential to commit suicide.

Aggression. For one subpopulation of chronic alcohol abusers (mainly young men), an increase in overall aggressive behaviors has been reported. A number of studies indicate that many of these individuals have an underlying antisocial personality disorder or an aggressive predisposition, which is exacerbated by chronic alcoholic drinking. In a study of men and women between the ages of twenty-one and thirty-five, subjects were randomly assigned to drink either an alcoholic or nonalcoholic beverage. The subjects were then engaged in a competitive task in which they could respond in an aggressive manner. The researchers found that among these individuals—both male and female—those with an aggressive predisposition were more likely to be aggressive in this competitive situation. For male subjects, however, the single greatest predictor of aggressive behavior was elevated blood alcohol concentration in conjunction with an aggressive predisposition.

Sex Drive. Although it is often assumed that alcohol increases sexual behavior, chronic excessive use has been found to decrease the level of sexual motivation in men. In some gay male populations, in which high alcohol consumption is also associated with increased high-risk sexual activity, this decrease in sex drive does not appear to result; however, for many chronic male drinkers, a long-term consequence of heavy drinking is reduced sexual arousal and drive. This may be the combined result of the decreased hormone levels produced by the heavy drinking and the decline of social situations in which sexual opportunities exist.

Cognitive Changes. Perhaps the best-documented changes in psychological function resulting from chronic excessive alcohol use are impaired cognitive functioning. While no evidence exists for any overall change in basic intelligence, specific cognitive abilities become impaired by chronic alcohol consumption. These most often include visuo-spatial deficits, language (verbal) impairments, and in more severe cases, memory impairments (alcoholic amnestic syndrome). A specific form of dementia, alcoholic dementia, has been described as occurring in a small fraction of

chronic alcohol abusers. The pattern and nature of the cognitive effects, as measured on neuropsychological assessment batteries in chronic alcohol abusers, exhibit a wide variety of individual patterns. Also, up to 25 percent of chronic alcoholics tested show no detectable cognitive deficits. Although excessive alcohol use has been clearly implicated in such deficits, a variety of co-existing lifestyle behaviors might be responsible for the cognitive impairments observed. For example, poor eating habits leading to vitamin deficiencies result in cognitive deficits similar to those observed in some alcohol abusers. Head trauma from accidents, falls, and fights (frequent experiences for heavy drinkers) may also produce similar cognitive deficits.

Therefore, it is extremely difficult to determine the extent to which the direct toxic effects of heavy drinking are responsible for the impairments—or if they are a result of the many alterations in behaviors that become part of the heavy-drinker lifestyle.

The specific psychological consequences of chronic drinking are complex and variable, but there is clear evidence that chronic abuse of alcohol results in frequent and often disastrous psychological and behavioral problems for drinkers and for those close to them.

See also **Aggression and Drugs: Research Issues.**

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ALCOHOL AND AIDS. Alcohol plays a role in virtually every aspect of HIV. Its use is connected with behaviors that lead to infection, makes infection more likely biologically, hastens disease progression, and interferes with adherence to treatment regimens and access to health care. Damage to the liver is often aggravated by infection with hepatitis B or C as well as effects of antiretroviral medication. The importance of these relationships led to the establishment of an AIDS research program at the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in 1987 (Auerbach et al., 1994). This entry presents evidence for the role of alcohol in each of these domains.

SEXUAL RISK BEHAVIOR

An ongoing debate regarding the relationship between alcohol use and sexual risk behavior is the difficulty—impossibility, even—of establishing a causal connection. Numerous studies have documented correlations between alcohol use in connection with sex and riskier sexual behavior. In one approach, overall drinking patterns are correlated with risky sex; information on typically significant relationships is obtained (reviewed in Cooper, 1992; Halpern-Felsher et al., 1996). Another commonly used strategy is to assess whether alcohol has been used in connection with sex and to correlate this with sexual risk. Again, information on significant relationships is generally obtained. Such correlations fail to establish causality; more convincing would be evidence that risky sex takes place only when alcohol is consumed, and not when it is not (see Leigh & Stall, 1993). In fact, even were these results to be obtained it would be impossible to rule out the explanation that people drink in order to feel relaxed enough to approach another person for sex.

Event-level studies take the approach of eliciting qualitative narratives regarding recent episodes of sex—usually both safe and risky—and analyzing the narrative for elements reflecting causal relationships (reviewed in Leigh, 2002; Weinhardt & Carey, 2000). Findings from these studies generally show that individuals who are safe when they are sober are also safe when they are intoxicated, with the exception that drinking at first intercourse was associated with decreased condom use.

More convincing regarding causality are experiments in which exposure to alcohol is systematically manipulated. Some investigators have sought to determine whether alcohol itself, or people's expectations of alcohol's effects, is responsible for risky behavior. These studies initially used a *balanced placebo* factorial design that enables separation of the effects of alcohol itself from expectancies regarding alcohol (reviewed in Hull & Bond, 1986; Leigh, 1989). Thus, if individuals have the expectation that alcohol will increase their sex drive or make them more socially relaxed, then they are likely to feel these effects. The literature relating alcohol expectancies to sex-related factors is limited. However, one interesting study randomly assigned 60 men to one of three arms: alcohol, placebo (belief that alcohol had been consumed), or sober (Gordon, Carey, & Carey, 1997). While alcohol itself impaired the men's ability to negotiate condom use during role plays relative to sober men, men in the placebo condition who had strong sex-related alcohol expectancies voiced more negative attitudes toward condoms.

Some experimental laboratory-based studies have compared the *disinhibition theory* of alcohol's effects with the *alcohol-induced myopia theory* (introduced by Steele & Josephs, 1990). Disinhibition theory asserts that alcohol releases one's more primal instincts that otherwise would be held in check by social propriety. Alcohol myopia theory predicts that because alcohol restricts the cognitive range of an individual, that person is likely to focus on salient elements in the environment, irrespective of their effects on socialized behavior; in this case, on whether they promote safe or unsafe behavior. In one article (MacDonald et al., 2000), four ingenious experiments were reported that were designed to pit these theories against each other. Results supported the alcohol myopia theory: Intoxicated participants in the impelling cue condition (toward risky sex) expressed significantly stronger intentions to have sex than those in the inhibiting condition, while no difference based on cue condition was observed for sober or (also sober) placebo participants.

In summary, evidence that alcohol is causally related to sexual behavior is strongest in the experimental studies. The last experiment described suggests, however, that, depending on which cues are most salient, alcohol use can lead either to risky or safe behavior, although the salient items in most sexual situations are likely to be more impelling than inhibitory. Among HIV-infected individuals, preventing risk behavior that may transmit the virus to others is made challenging by excessive use of alcohol (e.g., Purcell et al., 2005). This situation represents a significant public health problem.

IMMUNE FUNCTION

The deleterious effects of heavy and chronic use of alcohol on immune function in healthy individuals are well documented (reviewed in Cook, 1998; Isaki & Kresina, 2000). In HIV disease, heavy chronic use of alcohol is associated with a variety of immune deficits. Studies using animal models of HIV infection and human studies can be reviewed regarding this association.

Animal Studies. Much of the work on chronic alcohol abuse and rate of progression of HIV disease has been conducted in murine (mouse) or simian (higher primate) models. In these studies, animals are typically infected with an HIV-like retrovirus, given alcohol, and then challenged by exposure to another pathogen (infectious agent), often with assessment of immune indices. Such studies in murine models have demonstrated effects of acute alcohol consumption to reduce the synthesis and release of tumor cell necrosis factor (Nelson et al., 1990) and concomitant increased proliferation (rapid growth in number) of pneumonia-causing bacteria in the lungs (Nelson et al., 1990; Shahbazian et al., 1992).

Chronic alcohol consumption has also been shown to decrease host resistance to secondary infection and to impair immune function in a variety of ways in mice (reviewed in Dingle and Oei, 1997). Chronic alcohol administration resulted in

decreased CD8+/interferon-gamma+T lymphocytes, a fivefold increase in viremia (viral levels in the blood), and double the number of monocyte/macrophages in the brain (Potula et al., 2007). This cell type is the primary route of entry for HIV into the nervous system. Greater inflammation was observed in the brains of the alcohol-fed mice. In rhesus macaques infected with simian immunodeficiency virus (SIV), chronic alcohol consumption increased rates of viral replication (Poonia et al., 2006). These investigators obtained evidence that this effect may have been partially mediated by differential distributions of lymphocyte subsets in the intestine (Poonia et al., 2006). Monkeys chronically fed alcohol also exhibited more rapid disease progression (Bagby et al., 2006). In another SIV study, decreased caloric intake and metabolic dysregulation were observed along with depressed immune function (Molina et al., 2006).

Human Studies. Human studies are more difficult to conduct because many confounding factors can influence results, which may explain the much-greater number of animal studies. However, some approaches have been used to study effects of alcohol, both in vitro (in the test tube) and in vivo (in the live individual), on immune function among HIV-infected humans. Alcohol increases vulnerability to HIV infection in vitro. Lymphocyte proliferation following exposure to HIV peptides is reduced in the presence of alcohol (Nair et al., 1990), as is natural killer cell activity (Nair et al., 1994). A similar study, but in which blood was drawn prior to and following heavy drinking of participants, was reported by Bagasra and colleagues (1990). In another study using this model, HIV viral replication was enhanced in the presence of alcohol (Basgara et al., 1996). Interestingly, some of the immunologic effects of alcohol can be inhibited by administration of naltrexone, an opioid receptor antagonist frequently used in the treatment of alcoholism (Wang et al., 2006), suggesting its potential use as an adjunctive therapy for HIV-infected alcoholics.

In vivo, heavy substance use has been shown to be associated with increased viral load and lower CD4 counts (Lucas et al., 2002). While a strength of this study is that medication adherence was adjusted in the model (see following section on alcohol's effects on adherence), effects of alcohol use were not distinguished from those of other substances of abuse. A null effect of heavy drinking on cytokine (signaling proteins that are released by immune cells and that serve to communicate among cells) production was reported for patients co-infected with HIV and hepatitis C virus (HCV) (Graham et al., 2007). A study of HIV-infected patients initiating antiretroviral therapy found an inferior virologic response to treatment among those with a mood, anxiety, or substance use disorder; results for alcohol abuse or dependence (as indicated by *DSM-IV* criteria) were significant both for virologic rebound and virologic failure (Pence et al., 2007). Alcohol's effects on immune function in HIV disease may also increase the biological likelihood of transmission. A study of women showed that recent moderate-to-high levels of alcohol consumption (2 or more drinks the day before study participation) were associated with increased vaginal shedding of HIV-1 (Theall et al., 2008).

Researchers have wondered if the alterations in immunity caused by alcohol translate into more rapid disease progression. One study, taking into account alcohol's effects on adherence (see below) as well as immune function, modeled a simulation of HIV disease and estimated that hazardous drinkers (those who consumed five or more drinks at a sitting) lost three years of survival if they drank once per week, and 6.4 years if consumption was daily (Braithewaite et al., 2007). Another study followed 595 HIV-infected persons with alcohol problems (as specified by NIAAA; greater than 14 drinks per week or 5 or more drinks on a single occasion for men under 66 years; more than 7 drinks per week or four or more drinks on a single occasion for older men and all women) prospectively for seven years, assessing CD4 counts and viral load levels, controlling for confounders such as depression and medication adherence (Samet et al., 2007). They found that among patients not receiving antiretroviral therapy, heavy alcohol consumption was associated with a lower CD4 count but not higher viral load compared with abstinent subjects. For patients on antiretroviral therapy, heavy alcohol consumption was not associated with different levels of either marker.

Thus, results using animal models show consistently that alcohol consumption is associated

with depressed immunity. The results for humans are less consistent, and more research, particularly research to identify mechanisms for effects, will be helpful.

Adherence to Treatment. In the mid-1990s, highly active antiretroviral treatment (HAART) became available and changed the lives of many people with HIV from living with a death sentence to living with a manageable chronic disease. Adherence to these treatments is vital both to prolong patients' lives and to prevent mutation of the virus to become resistant to the drugs. As treatment regimens have gotten simpler—HAART medications can be taken as a single pill as of 2008—adherence has become easier, but non-adherence is still common. Alcohol use and abuse have proven to be a barrier to medication adherence across a variety of studies. Non-adherent (operationalized as less than perfectly adherent) men and women in one study were distinguished only by alcohol-related factors such as greater number of drinks (Parsons et al., 2007**).** One longitudinal study that followed 3,761 men and women for five years found hazardous alcohol use (defined by NIAAA as in the study above) to be independently (of many sociodemographic factors) associated with decreased ART utilization, 2-week adherence, and viral suppression (Chander et al., 2006). Another large longitudinal study followed cohorts of men and women receiving treatment (Lazo et al., 2007). Participants were followed for five years and underwent assessment of psychosocial factors, including drinking, and adherence every six months. Adherence was predicted by the presence of depression in men, and the occurrence of binge drinking in women. This study is unique in that it identified some sex-specific barriers to adherence. Another multi-faceted study used backward regression analysis to identify a parsimonious model of adherence (Holstad et al., 2006). The final model included abstinence from alcohol.

Physical and psychological trauma and alcohol abuse proved to be a barrier to adherence in another study (Mugavero et al., 2006). Correlates of non-adherence, defined as having missed any doses over the prior seven days, was predicted by the number of categories of lifetime traumatic events, the Addiction Severity Index alcohol score, and being uninsured. While psychological depression was not assessed in this study, the results point to the *nexus of risk* (O'Leary, 2001) that characterizes the lives of many people who become infected with HIV. Indeed, depressive symptoms and major depressive disorder were extremely prevalent in a study of HIV patients with substance use disorders (Berger-Greenstein et al., 2007). Depression and alcohol use are well known to be linked (Dorus et al., 1987), and depression predicts relapse after drinking cessation (Kodl et al., 2008). Trauma, mental health problems, addiction, and sexual risk are so often intertwined in these individuals' lives that it is difficult to establish a single factor as causative of infection or failure of adherence.

An intervention study was designed to improve adherence and reduce drinking among 143 hazardous drinkers in New York (Parsons et al., 2007). At a three-month follow-up, adherence was significantly higher, and viral load and CD4 count had improved. However, no significant effects on drinking were observed, and at a six-month follow-up none of the outcomes was statistically significant.

Misuse of alcohol has a substantial impact on HIV-infected patients' ability to adhere to their medical regimens. One intervention study showed somewhat promising effects; more work to reduce or eliminate alcohol use among HIV patients is needed.

ORGAN DAMAGE

The organs most vulnerable to alcohol-induced damage, the liver and the brain, are also challenged by HIV disease and treatment. Further, many individuals with HIV are co-infected with hepatitis C or B (HCV; HBV) due to previous needle-sharing or sexual behavior. Among HIV-infected persons, HCV is considerably more common than HBV. Both of these viral infections often lead to fibrosis, cirrhosis, and death. HIV itself hastens progression to end-stage liver disease among HCV-infected patients (Graham et al., 2001). In patients co-infected with HIV and HCV, heavy alcohol use is associated with more rapid progression of liver disease (Benhamou et al., 2001; Castellares et al., 2008; Cooper & Cameron, 2005; Pol et al., 1998) and mortality related to liver disease (Salmon-Ceron et al., 2005). However, many studies designed to identify predictors of liver disease in co-infected patients have not assessed alcohol use, and it is unknown as of 2008 how frequently their healthcare

providers assess and/or intervene to reduce their drinking. It is interesting to note that HIV-positive individuals who learn that they are co-infected with hepatitis reduce their drinking, possibly because their providers have counseled them to do so (Tsui et al., 2007). It has been recommended that co-infected patients abstain from alcohol altogether (Conigliaro et al., 2006).

Alcohol affects the nervous system in healthy individuals, particularly in the context of chronic alcoholism. The most commonly observed deficits are in abstract thinking ability, complex perceptual-motor skills, and learning and recall (for a review, see Grant, 1987). HIV crosses the blood-brain barrier (Nottet et al., 1996), and since most therapies do not, viral replication takes place there relatively unchecked (Ellis et al., 2007). Prior to the advent of HAART, about 30 percent of AIDS patients developed AIDS dementia complex, accompanied by the loss of up to 40 percent of neurons (Dickson, 1986; for recent reviews see Anthony & Bell, 2008; Hult et al., 2008). In HIV-infected patients, alcoholism is associated with altered brain morphology (Pfefferbaum et al., 2006) and works synergistically (having a multiplying effect) with HIV infection to damage white matter in the brain (Pfefferbaum et al., 2007). Alcohol and an envelope protein of HIV (gp120) act in concert to increase the permeability of the blood-brain barrier, induce stress fiber formation, and inhibit the formation of reactive oxygen species (ROS) (Shiu et al., 2007). ROS prevents oxidative damage that can lead to cognitive dysfunction. Alcoholism and HIV infection can produce neurocognitive deficits that neither does alone (Sassoon et al., 2007).

Chronic abuse of alcohol is damaging to the liver and the central nervous system. In some cases, alcohol potentiates (causes a multiplying effect on) the negative effects of HIV infection in both organs.

SUMMARY

This review has provided evidence that alcohol negatively influences many aspects of HIV. It is associated with elevated sexual risk behavior, which may lead to infection or transmission. It produces negative effects on immune function and disease course. It is associated with reduced adherence to medical regimens, giving rise to elevated viral loads and the potential for the virus to develop resistance to medications. Finally, it shortens the time to liver damage and mortality among patients co-infected with hepatitis. It also worsens neurocognitive dysfunction. Given all of these negative consequences, and recommendations that drinking be reduced or eliminated for HIV-positive persons, the paucity of interventions designed as of 2008 to reduce alcohol use in this population is surprising. Care providers should be encouraged to assess alcohol problems, which can be done easily with the approach described in the online NIAAA Clinician's Guide, and to intervene in the step-by-step manner presented in the Clinician's Guide four-item CAGE (Samet et al., 2004). Providers should be encouraged to identify and intervene with alcohol problems in their patients, and educated on how to do so. More attention to alcohol abuse should be paid by providers, and improved interventions to reduce or eliminate drinking by HIV-infected patients should also be developed, tested, and disseminated.

See also **HIV Risk Assessment Battery (RAB); Substance Abuse and AIDS.**

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ALCOHOL- AND DRUG-EXPOSED INFANTS.

Since the 1970s, increasing recognition of the use of alcohol and drugs by women during pregnancy has led to concern for possible deleterious effects to the developing fetus. With the greater societal acceptance of drug use that began in the 1970s and the development of smokable forms of drugs that were formerly only used by injection, women of childbearing age and pregnant women dramatically increased their use of alcohol and other substances.

SUBSTANCES USED BY PREGNANT WOMEN

Tobacco and alcohol are the most commonly used drugs during pregnancy. In the United States, tobacco exposure complicates 25 percent of all pregnancies, and alcohol, although widely recognized as causing harm to the fetus, is consumed by about 20 percent of pregnant women. Illicit drug use occurs in about 5.5 percent of all pregnancies, a figure that may be an underestimate as national surveys are based on self-report. Based on these data, about 450,000 pregnancies annually are complicated by drug exposure and approximately 820,000 by alcohol exposure in the United States. Among illicit drugs, marijuana is most frequently used, followed by cocaine. Crack use, cocaine in its smokable form, became an epidemic in the 1990s among poor, urban women. Heroin, methamphetamine, methylenedioxymethamphetamine (MDMA, Ecstasy) are also used during pregnancy, as well as phencyclidine (PCP), ketamine, and LSD, but to a lesser extent.

Additionally, legal drugs, such as methadone and buprenorphine, may be prescribed for treatment of heroin addiction during pregnancy, and the burgeoning use of antidepressants during

pregnancy has resulted in identification of SSRIs (selective serotonin reuptake inhibitors) as potentially harmful to fetal development. Anti-epileptic drugs are also medically prescribed during pregnancy when necessary. Nicotine-replacement therapy is often recommended during pregnancy, though concerns exist about the injurious fetal effects of the drug.

FETAL IMPACT OF MATERNAL USE

The majority of alcohol dependent and drug-addicted women use multiple substances. Since all drugs are carried across the placenta from mother to fetus, the newborn (neonate) is frequently exposed to a multiple-drug cocktail. The clinical condition of the newborn and infant long-term development depend on the type of drugs used, the frequency, amount, duration, trimester of use, and the time since last use. Since embryonic and fetal development unfolds in an orderly fashion, first trimester exposure may affect physical and organ development, whereas third trimester exposure may affect brain processes while leaving physical development unaffected. Thus functional impairment may exist with normal anatomic development.

Newborns recently exposed to heavy alcohol, heroin, methadone, or other opioids during pregnancy may experience withdrawal, or neonatal abstinence syndrome. Alcohol withdrawal symptoms occur generally within twelve hours of birth; opiate withdrawal symptoms may be delayed up to a week but tend to occur within forty-eight hours. Methadone withdrawal symptoms may not occur for as long as two weeks.

The Finnegan Scale, created by Loretta Finnegan, was devised to measure symptoms of withdrawal, which include irritability, tremor, and increased muscle tone. Other symptoms include jitteriness, high-pitched cry, poor feeding, seizures, vomiting, diarrhea, apnea (suspension of breathing), sweating, frequent yawning, sneezing, symptoms of fever, and sleeping difficulties. Drug-exposed newborns frequently present with prematurity, low birth weight, or intrauterine growth retardation (IUGR), drug or alcohol related birth defects, or facial dysmorphism that signal the need to monitor for withdrawal symptoms. For heroin or opioid exposed infants, withdrawal occurs in 55 to 94 percent of infants. Heroin exposure withdrawal symptoms can persist for about ten days postnatally whereas those associated with methadone can last up to eight weeks.

MANAGEMENT

A thorough alcohol and drug use history should be obtained from the expectant mother and should be corroborated by testing the urine of both mother and newborn for alcohol and other drugs. Drug assessment of infant meconium can detect drug use during the last two trimesters of pregnancy, in contrast to the twelve-hour to two-week window apparent through urine screening. Newborns should be closely monitored for signs of withdrawal for a minimum of forty-eight to seventy-two hours and longer when the mother has been on methadone maintenance treatment. Since symptoms of withdrawal are nonspecific and may be confused with a variety of infections or metabolic disturbances, a search for concurrent illness to explain symptoms is also mandatory.

Most hospital nurseries use a standardized neonatal abstinence syndrome scoring system such as the Finnegan Scale. The hospital monitors the neonate's sleep habits, temperature, and weight. The earliest withdrawal symptoms are treated by intravenous fluids, swaddling, holding, rocking, a low-stimulation environment, and small feedings of hyper-caloric formula for weight gain. If symptoms continue or increase, medication may be initiated. Common medications include camphorated tincture of opium (Paregoric) or phenobarbital for opioid withdrawal, Phenobarbital or Diazepam for alcohol withdrawal. Diazepam is also used to help with cocaine hyperexcitability.

Interviewing the exposed mother is essential in evaluating the anticipated home environment and the extent of maternal addiction or dependence. Unfortunately, infants exposed to drugs and alcohol in utero are often at high risk for abuse and/or neglect. Normal maternal-infant bonding is difficult in the case of an irritable, poorly responsive neonate and a mother dealing with guilt, low self-esteem, poverty, inadequate housing, and an abusive or absent partner or parent, all of which often accompany her own drug addiction. A referral to child protection services may therefore be indicated.

Women who use drugs or alcohol during pregnancy are also highly likely (50%) to have significant mental health problems, especially depression and anxiety requiring referral, and a history of sexual abuse. Domestic violence is often present, especially with illicit drug use that involves criminal activity. The Drug Abuse Screening Test (DAST) or the Michigan Alcohol Screening Test (MAST) can be useful in establishing the extent of drug and/or alcohol dependence. The TWEAK alcohol screening test—an acronym for Tolerance, Worried, Eye-opener, Amnesia, and Kut down (as in "cut down consumption")—consists of five questions and was developed to screen pregnant women for harmful drinking habits. The involvement of social services for follow-up is paramount to ensure the health of both mother and infant. Breastfeeding is contraindicated as drugs and alcohol pass readily to the infant through breast milk. A significant percentage of drug-exposed or heavily alcohol-exposed infants need foster care placement. Infants whose parents are addicted to tobacco, crack-cocaine, marijuana, or methamphetamine are at risk for continued drug exposure in the home environment.

Alcohol and substance abuse during pregnancy are related to a higher risk for medical or obstetric complications, including high blood pressure, poor nutrition, sexually transmitted diseases, and preterm birth. Risk of human immunodeficiency virus (HIV)/AIDS is also high. Lack of, or inadequate, prenatal care and mental health problems are common. Obstetric management is complex, and substance abuse treatment, mental health, and social services coordinated with prenatal care are necessary.

OUTCOME

Research studies beginning in the 1970s with the identification of Fetal Alcohol Syndrome (FAS) and cresting in the 1990s with the crack-cocaine epidemic resulted in a growing body of literature on the negative effects of alcohol and drugs on child developmental outcomes.

Alcohol is the most widely used human teratogen, the leading cause of birth defects, and one of the leading causes of mental retardation. FAS, characterized by growth deficiency, mental retardation, and facial dysmorphology, affects two thousand to twelve thousand U.S. children a year. Many more prenatally alcohol-exposed children have varying degrees of learning disabilities and motor, behavioral, or physical problems, categorized broadly as Fetal Alcohol Spectrum Disorders (FASD).

There is no known safe dose of alcohol exposure during pregnancy. Low-to-moderate prenatal exposure has been associated with Attention-Deficit Hyperactivity Disorder (ADHD), visual-motor problems, learning and memory impairment, poorer information processing speed, and IQ decrements at school age. Adolescents and adults prenatally exposed continue to demonstrate these problems as well as social behavioral deficits. The amount and duration of prenatal exposure are related generally to the severity of problems seen. By 2008 imaging studies had begun to document reductions and alterations in specific brain areas associated with prenatal alcohol exposure and the impairments found in alcohol-exposed offspring.

Tobacco accounts for more cases of Sudden Infant Death Syndrome (SIDS) than all other abused substances, and is the major environmental cause of low birth weight. Maternal smoking during pregnancy does not appear to be related to infant malformations but has been related to long-lasting deficits in child cognitive function. Prenatal tobacco exposure has been related to infant visual and hearing impairments, childhood ADHD, and delinquent behaviors and poor educational attainment in adolescence and adulthood. Continued exposure to passive smoke in the household should be considered an additional risk factor affecting child behavior.

Marijuana is the most commonly used illegal drug during pregnancy. Two prospective cohort studies in Pittsburgh and Ottawa looked at the relationship between heavy marijuana exposure and outcome. As with alcohol and tobacco, marijuana exposure was related to attentional and behavioral problems, including delinquency. Short-term memory and visual reasoning problems were seen in the preschool years, and poor ability to organize and integrate cognitive information and poorer visual-perceptual skills were evident by nine to twelve years. Attentional problems appeared to resolve by adolescence. Depressive symptoms were also found to increase at school age.

The majority of cocaine-exposed infants are exposed to multiple substances, primarily alcohol, tobacco, and marijuana, so research has attempted to differentiate cocaine effects from those of other drugs through large prospective cohort studies. No cocaine syndrome with consistent dysmorphology had been identified as of 2008. Cocaine exposure has been related to behavioral problems, jitteriness, sleep dysregulation, excitability, poor feeding, and poor visual attention in the neonatal period. Greater risks of infectious diseases, SIDS and, for very low birth-weight preterm infants, a higher incidence of vascular hemorrhage have been found.

Long-term follow up studies to school age cocaine-exposed children reveal persistent language and attentional problems, identifiable as early as one year of age. Visual-motor and visual-reasoning deficits to school age have been linked to the extent of exposure. Studies of behavioral outcome have been inconsistent but have suggested increased aggressive and delinquent behavior. Although specific deficits have been noted related to the severity of prenatal cocaine exposure, the early alarmist and media reports in the 1990s of the hopelessly damaged crack baby have proved to be erroneous.

Heroin and methadone are the most commonly used opiates during pregnancy, affecting about ten thousand infants annually in the United States. Opiate exposure does not appear to be related to structural abnormalities among offspring, although neurobehavioral abnormalities may last up to six months postnatally. Follow-up of small samples of children prenatally exposed to heroin or methadone at school age indicate a higher rate of conduct disorder and lower school achievement than non-exposed children.

Methamphetamine is the most widely used stimulant drug in the world. A Swedish study that followed methamphetamine-exposed children to fourteen years found them to have delayed math and language development, peer behavioral problems, and poorer physical fitness compared to norms. Exposure to methamphetamine fumes in the home is also a concern for developmental toxicity.

There are no long-term studies, as of 2008, on PCP or MDMA, although studies were under way. The caretaking environment of the drug- or alcohol-exposed child is often not optimal, because of maternal addiction, also contributing to poorer child outcomes. Screening and treatment for substance use and mental health disorders among pregnant women are paramount in order to reduce the morbidity associated with prenatal drug and alcohol exposure.

See also **Fetal Alcohol Syndrome; Fetus, Effects of Drugs on the; Pregnancy and Drug Dependence.**

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ALCOHOL- AND DRUG-FREE HOUSING.

Alcohol- and drug-free (ADF) housing, also called sober housing, sober-living environments, or alcohol-free living centers, provides accommodation for people who choose to live free of alcohol and/or drugs. ADF housing is ordinary housing located in residentially zoned areas, in architecture that includes single-family housing, multi-family housing, apartment complexes, and shared housing (co-housing).

DEFINITIONS AND PRINCIPALS

ADF housing provides domestic settings to support residents' day-to-day efforts to maintain sobriety. Nearly all residents in ADF housing are recovering from alcohol/drug problems. The residents come from myriad social and economic backgrounds. Most attend AA or NA meetings; many are participants and clients in the community's health, education, and social services; some residents are involved in the justice system. The house might include a few residents who prefer sober living for reasons not related to personal alcohol/drug problems.

The house itself is the service that supports sobriety. The house is managed in whole or in part by the residents, and no clinical or counseling services are provided on-site. Although residents often attend these services off-site, providing them on-site could seriously defeat the purpose of ADF housing in two ways. First, the housing would lose the protection of Fair Housing Amendments Act of 1988 (FHAA) regarding rights to live in any residentially zoned area and personal privacy under the Fourth Amendment. Second, the housing would lose its efficacy to support personal choices to maintain sobriety.

The FHAA prohibits housing discrimination by allowing people with disabilities to live together for a shared purpose such as mutually assisted recovery and maintenance of an abstinent lifestyle. The act expands protections of family housing to include people in recovery not related by blood or marriage. Practically speaking, this means state and local jurisdictions cannot establish limits on numbers of persons occupying the house or upon lengths of stay that do not apply to all residences in the community. Additionally, state or local jurisdictions cannot impose licensure or certification requirements that do not apply equally to all residential land-uses in the community (American Planning Association).

FHAA protections are likely to be lost if formal counseling, education, or other non-residential services are provided on-site. Limited services can be provided that would reasonably be provided in any residence, such as visiting nurse services or in-home tutoring. The test is whether a local or state jurisdiction could insist the facility be zoned and licensed consistent with state and local standards for the delivery of such services. Without protection under the Fair Housing Amendments Act, experience shows that local communities exclude ADF residences from safe and economically stable areas most conducive to recovery. In California, for example, as of 2008 the state and several cities were pursuing legislation to restrict numbers of residents, restrict locations, and impose intrusive inspection and drug-testing requirements on sober-living facilities (Sober Living Network).

Equally important to protection of basic housing rights is protection of ADF housing as a setting for recovery and sober living. The capacity of the house to support day-to-day alcohol-free living, including oversight by management and occasional house-calls, would be compromised if non-residential services were provided on the premises, just as the quality of private family life would be infringed by having to accommodate non-family uses in a private family home. Service providers, referral sources, and benefactors who rely on ADF housing usually understand this separation and respect the primary rules under which every sober-living house operates: (1) residents remain sober at all times (no drinking or drug use); (2) residents pay their rent on time; and (3) residents participate in house rules relating to daily living, such as housekeeping, clean-up, guest policies, curfews, and participation in house meetings. (Kaskutas, 1999).

Increasing numbers of research studies indicate that such ADF residences extend residents' sobriety, improve their income, and reduce service utilization (McCarty et al., 1993). Studies also find that ADF housing benefits a variety of residents from many backgrounds, including people who have been in jail (Polcin, 2006). As of 2008, work was under way to investigate the utility of various ADF housing forms to meet the needs of various groups and determine which groups do well in which settings (Kaskutas & McLellan, 1998). Answers to these questions can calibrate housing design and operations. Answers can also help strengthen quality standards so the most promising examples can expand reliably, which is important in order to meet the rising demand for ADF housing.

FEATURES OF ADF HOUSING

ADF housing first appeared with the temperance movement in the 1830s, and the architecture of sober housing has operated within national patterns of residential accommodation for low-income renters since that time. As the U.S. urbanized, communities provided sober accommodation in rooming houses and hotels whose proprietors did not permit their boarders or renters to drink on the premises. As suburbs developed and single-family homes became the norm, architecture for ADF residences included houses originally designed to accommodate families or individuals living independently. Current forms of sober housing include single-room occupancy (SRO) hotels, rooming houses, single-family houses, and multi-family housing. These forms of sober housing have emerged alongside the growth of the twelve step recovery movement, which started in the late 1930s. Although the AA does not own or operate sober housing, most operators are highly sympathetic to AA (some require attendance at AA meetings), and many AA members depend upon sober housing as part of their daily recovery regimen.

Freestanding, independent sober residences were able to function quietly in large cities until redevelopment turned toward city centers in the 1960s and 1970s, destroying large amounts of low-income housing. SROs were particularly devastated. The independent recovery community lost access to low-income housing and to new housing opportunities. Only independently owned ADF facilities already in operation were able to continue.

ADF Service Models and Supporting Organizations. Starting in the 1970s and 1980s, recovery-oriented ADF housing differentiated into three basic models, each with its own association: resident-run housing; peer-based entrepreneurial sober housing networks; and program-affiliated sober housing. Healthy competition has developed among these models.

Oxford Houses are resident-run housing established by middle-class professionals in recovery who seek large resident-run single-family facilities in the suburbs and other desirable residential areas. Oxford Houses operate according to a charter drawn up by a few founding Oxford House residents in the mid-1980s (Oxford House, 1988). Having benefited from federal legislation providing small start-up grants, Oxford Houses were estimated as of 2008 to include about one thousand facilities in the United States and Europe.

In the peer-based entrepreneurial model, ADF housing relies on property managers/owners of ADF housing, many of them in recovery themselves, to create their own organization. This organization sets its own standards and provides its own governance to assure close adherence to ADF housing principles. For example, the Sober Living Network in Los Angeles has about 250 member-houses, according to its Web site.

Program-affiliated ADF facilities operate according to a step-wise progression of accommodation, rules, and expectations designed to promote successful movement into recovery. Some of these programs function as several sober residences linked together by central management (Beacon House, San Pedro; Sun Street Center) or loosely linked by geography in proximity to recovery services and neighborhood social centers (Los Angeles neighborhood recovery centers). Other programs operate sober residences in connection with other off-site program activities that provide counseling, vocational, and health/social services (Escondido program, VOA, Salvation Army). In California approximately one hundred ADF houses, called Sober Living Environments or SLEs, belong to a statewide association that advocates their interests with the state alcohol/drug agency and the state legislature (California Association of Addiction Recovery Resources, 2008).

Operational Configuration. Recovery-oriented ADF facilities operate with great flexibility through a system of interconnected axes (Wittman, 1993). This system lets ADF housing follow basic principles consistent with community resources of housing stock, the recovery population seeking ADF housing, and relationship to public agencies providing AOD-related professional services.

ADF facilities may vary in size from a few people living in a single-family home to more than one hundred rooms in a residential hotel that has been converted into a sober living facility. Thanks to FHAA protections, ADF facilities may be located in any residentially zoned area where affordable, accessible housing is available. The architectural design emphasizes domestic qualities that help

people relax and relate to each other in comfortable, informal, and natural settings.

Occupancy may be open to a variety of people in recovery and to abstainers or may focus on particular groups of people in recovery, such as employees, professional people, participants in a multi-component recovery program, people involved with the criminal justice system, or people grouped by age and gender. Also, house rules range from mandatory directives for all parts of life in the facility that all residents must follow to a framework with relatively few general rules designed to provide latitude for individual resident schedules and preferences.

ADF house management styles ranges from democratic, resident-run houses (Oxford Houses) to management by a founder and hand-picked successors (Sober Living Network) to managers selected by executives of the program operating the residence. Also, some ADF residences are free-standing business entities operating as a private corporation, either for profit or not-for-profit. Other residences are tied to AOD treatment/recovery programs, to other health and social service providers, and to other organizations that provide ADF accommodation for their members, such as colleges with sober-housing dormitories. Additionally, some ADF housing occupies the entire facility, such as a single-family house dedicated to sober living. Other ADF housing shares facilities with compatible uses, for example, ADF housing upstairs with nonalcohol commercial activities on a ground level.

CHALLENGES

The following ADF housing challenges appear and re-appear in various forms over the years.

Demonstration of effectiveness. Well-run ADF facilities have functioned well on face validity as residents and ADF housing managers conscientiously support recovery (maintain sobriety) and operate with great sensitivity to neighborhood concerns. However, as federal support for community alcohol and drug programs in the early 2000s requires evidence-based results and accountability, state alcohol and drug program agencies are beginning to ask for formal evaluations of ADF facility operations. Pathbreaking qualitative research done in the 1990s to describe the utility of sober residence operations in terms of resident experiences (Kaskutas & McLellan, 1998) was in the early 2000s being supplemented with quantitative analysis that calibrates the performance of ADF settings (Polcin, 2006). These findings are being used to help set clearer standards for quality operation.

Capacity to Accommodate New Groups. The recovery movement attracts groups with a variety of drinking/drug problems, including those with mental disabilities, nonviolent offenders, and general population groups such as college students and employees. In practice, ADF housing operators have long accommodated residents from these groups on an individual basis as circumstances permit. However, as residential facilities to serve the mentally ill evaporated, as prisons became overcrowded, and as affordable housing for low-income people withered, pressures mounted on ADF settings to provide accommodation for special-needs residents.

The demands of dual-need and multi-need groups test the limits of ADF housing. Sponsoring agencies that provide services to the dual-diagnosed mentally ill, for example, do not share ADF housing requirements for strict sobriety and use of off-site services. Many agencies providing services for chronic inebriates with mental health problems prefer a harm reduction approach using supportive housing rather than an abstinence model (CSH references). Supportive housing allows residents occasional slips and provides on-site services. Similarly, drug-testing and reporting requirements introduce complications for accommodation of parolees and offenders under court supervision. Although these circumstances contradict basic house policies regarding sobriety and on-site services, some ADF residences go part way to accommodate some residents with special needs. A few ADF residences follow a so-called damp policy that does not allow drinking on the premises but permits off-site drinking within limits.

Despite differences in philosophy, supportive housing and sober housing have similar residential architecture requirements, as noted below. Thus it is possible for some cities to experiment with so-called wet housing under a harm reduction approach that allows chronic homeless inebriates in a high-density urban area to drink in their rooms and to obtain

counseling and health services on-site (Downtown Emergency Service Center). This housing first approach provides a safe environment for someone who would otherwise continue a long history of high service utilization and nuisance behavior. This approach is a community-level (municipal) response to the dearth of federal- and state-supported action to meet housing needs of such groups with high service needs, including offenders being released from prison and young people graduating from the foster care system (Pearson et al., 2007).

Economic Viability. The basic economic model for ADF house operation, as for any ordinary residence, depends on payment of rent or a mortgage. Financial operation of ADF housing is based nominally on standard housing market factors. However, ADF residents in recovery usually are below-average earners who are not able to pay full market rents.

One problem is how to make ADF housing economically viable for ADF residents who cannot afford standard market rates. In the Oxford House model, residents share the cost of renting the house to create affordable accommodation in a market-rate environment at a modest per-person cost. Otherwise, answers depend on making a case to win support from public and foundation/personal supporters that find the investment attractive. Public support for ADF housing must compete with other public-housing alternatives such as conventional low-income housing and supportive housing. Public funding also invites public oversight that may challenge the very foundations of ADF housing. Foundation and personal giving approaches target foundations and individuals (such as house alumni) who are especially attracted by ADF housing values and able to give back in appreciation for the help they received personally.

Community Resistance. Neighborhood resistance (Not In My Back Yard, or NIMBYism) remains a continuing challenge for ADF housing to be met in two ways. While firmly insisting that local authorities uphold recovering people's rights to housing, ADF operators further recognize the importance of outreach and responsiveness to neighborhood concerns. This responsiveness includes being accessible and participating in neighborhood activities (neighborhood clean-ups, block parties, neighborhood safety campaigns, holiday celebrations). Outreach to engage neighbors provides opportunities to debunk concerns based on fears, misperceptions, ignorance, rumors, and incorrect information. There is no evidence to show that ADF housing increases crime or decreases property values; sometimes the opposite occurs in distressed neighborhoods. Neighborhood disturbances and confrontations rarely occur at well-run houses. The antidote to NIMBY concerns is outreach and contact with the neighbors rather than increased surveillance by law enforcement or more inspections by public officials.

Architectural Quality. Architecture for ADF facilities (design and use of settings to help people jointly maintain their sobriety day by day) is critical to program and financial success. Design features deeply influence how residents feel about themselves, how they perceive each other, and their attitudes toward living sober. These feelings, perceptions, and attitudes translate into personal behavior and group expectations. These features can be measured and evaluated, and researchers and ADF operators could do more to explore effects for recovery experiences and outcomes. The following are some suggestions:

- Location of the facility needs to be in a safe area, accessible to public transportation.
- The facility perimeter needs to be secure and entry needs to be controlled to manage the occupancy of the house and to discourage contraband.
- The circulation system needs to bring people together in socially spontaneous ways (sociopetal) rather than to keep them apart in ways that encourage isolation (socio-fugal).
- The house needs a room large enough for all residents to gather for regular house meetings.
- Residents need their defined sleeping space, including lockable storage, that provides some privacy and separation (protection) from other residents.
- Outdoor areas, views, and plants are vital to support human needs for contact with the rhythms of daylight and the passage of time and contact with sunlight.
- Quality fixtures and furnishings are vital to effective operation, how residents feel about themselves, and how they view each other.

The house should be fully maintained and kept clean, and all equipment should be safe and in good repair as a matter of respect and functionality. Fire safety and building codes need to be met, or an upgrade plan needs to be in place.

Well-maintained and attractive houses help create support among neighbors.

Certification. High standards, followed with great fidelity by each facility, are critical to successful ADF housing. Traditionally certification has been experiential and word-of-mouth, residing within the personal integrity of well-known housing managers operating houses in close-knit local communities.

As ADF housing operations expand from the personal to an organizational basis, it is necessary to assure high-quality operation for each house. The challenge for the traditional craft of ADF management is responding to rising demands for accountability, organizational complexity, and new electronic operating technologies. In California, two perspectives are contending with each other. The tradition of owner/manager responsibility for the house is being expanded to peer-based oversight in which an association of residents (Oxford House) and/or on-site managers (SLN owner/operators) hold their members accountable for high-quality operation. Alternatively, a modern professional-technical perspective seeks to create statewide licensing standards, with input from residents and house-managers, to be overseen by public agencies at the state and local level (California State Department of Alcohol and Drug Programs; California Association of Addiction Recovery Resources, 2008).

These two approaches head in opposite directions. Either ADF housing operators create a peer-based certification system recognized by the state, or the state certifies ADF housing with input from the ADF housing community to help write standards and licensing procedures. The former approach supports the experiential foundation of the recovery-based sober housing movement and falls under the Fair Housing Amendments Act. The latter approach supports the notion that the state is responsible for operating standards to protect the public and ADF housing residents. Advocates for peer-based certification vigorously object that requirements for public agency oversight will create a special class of licensed housing that loses protection under the FHAA, resulting in restrictive local zoning controls and intrusive inspections. They also argue there is no reason to believe that state controls on ADF residences will achieve better results than resident-run or peer-managed houses, and there are concerns that state controls will suppress self-supervision and innovation, replacing them with a cumbersome, nonresponsive and ineffectual state bureaucracy.

ADF housing may find itself a niche as its full value comes to be appreciated, which was happening in the early 2000s as new populations sought out ADF housing in the absence of other appropriate residential accommodation. As demand for ADF housing grows, two forces were expected to shape its movement in positive ways. Growing research and evaluation was anticipated to provide useful feedback, and organizational growth was anticipated to expand the traditional focus on operation of individual houses to include shared operating standards.

As of 2008, however, the ominous question of who would control ADF housing remained unanswered. It might continue to be resident-run/peer-managed, with primary focus on the identify and quality of the individual house, or control might shift to public agency supervision by state and local agencies with primary focus on operation of a certification system, The answer goes to the heart of ADF concepts and their political expression at the community level. A number of observers, including many ADF housing providers, believe that state supervision would abridge FHAA protections leading to loss of locations and housing stock and to imposition of unworkable restrictions. As the battle for controlled continued, peer-entrepreneur ADF housing operators considered taking legal action to maintain protection under the Fair Housing Amendments Act.

See also **Treatment: A History of Treatment in the United States.**

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ALCOHOL, SMOKING AND SUBSTANCE INVOLVEMENT SCREENING TEST (ASSIST).

The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) was developed under the auspices of the World Health Organization (WHO) by an international group of specialist addiction researchers and clinicians in response to the public health burden associated with problematic substance use worldwide. The ASSIST was designed to screen for problem or risky use of tobacco, alcohol, cannabis, cocaine, amphetamine-type stimulants (ATS), sedatives, hallucinogens, inhalants, opioids and "other drugs." A risk score is obtained for each substance and falls into either a "low," "moderate," or "high" risk category. This determines the type of intervention, "none," "brief intervention," or "brief intervention plus referral."

See also **Diagnosis of Substance Use Disorders: Diagnostic Criteria; Treatment, Stages/Phases of: Screening and Brief Intervention.**

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ALCOHOL USE DISORDER AND ASSOCIATED DISABILITIES INTERVIEW SCHEDULE.

See **AUDADIS.**

ALCOHOL USE DISORDERS IDENTIFICATION TEST (AUDIT).

Originally developed as the result of a World Health Organization (WHO) collaborative project among six countries—Australia, Bulgaria, Kenya, Mexico, Norway, and the United States—the Alcohol Use Disorders Identification Test (AUDIT) is a screening instrument designed to assess hazardous or harmful alcohol consumption (Saunders, Aasland, Babor, De La Fuente, & Grant, 1993). Due to the cross-national study from which it originated, the AUDIT holds the distinction of being the first alcohol screening instrument specifically designed for international use (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001). Screening refers to the administration of a questionnaire to estimate the

	Response scale & scoring				
Item 1	Never	Monthly or less	2–4 times/month	2–3 times/week	4 or more times/week
Item 2	1 or 2	3 or 4	5 or 6	7–9	10 or more
Items 3–8	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
Items 9–10	No		Yes, but not in the last year		Yes, during the last year
	0 Points	1 Point	2 Points	3 Points	4 Points

Table 1. Response scale for each of the 10 AUDIT items and designation of the point value associated with each response. (Adapted from Saunders, Aasland, Babor, De La Fuente, & Grant, 1993.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

probability that a specific condition exists among members of a population. While screenings are intended to provide insight into the people who are likely to have a disorder, these instruments do not establish a definitive diagnosis (Stewart & Connors, 2004; 2005).

INSTRUMENT CONSTRUCTS AND CONTENT

The AUDIT represents an early intervention tool. More specifically, the AUDIT is intended to identify a broad spectrum of problem drinking before significant harm or dependence may develop. Overall, three constructs are examined by this 10-item instrument: hazardous alcohol use, alcohol dependence symptoms, and harmful alcohol use.

Hazardous Alcohol Use. The first three questions of the AUDIT assess the domain of hazardous alcohol use. One's drinking behavior is considered hazardous when the *risk* of harmful physical and/or psychological consequences is increased (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001). Overall, this section measures one's alcohol consumption behaviors by assessing the frequency of drinking alcohol (Question 1), the typical quantity of alcohol consumed daily (Question 2), and the frequency of heavy drinking (Question 3). It is important to note that the AUDIT determines heavy drinking to be the consumption of six or more drinks, as based upon European standard drink sizes. The U.S. equivalent to this standard for heavy drinking would be five or more drinks. Consuming five or more drinks in one sitting is often referred to as binge drinking (Wechsler, Davenport, Dowdall, Moeykens & Castillo, 1994). Accordingly, a heavy drinking cut-off of four or more drinks should be utilized to determine heavy drinking among women (Wechsler, Dowdall, Davenport & Rimm, 1995).

Alcohol Dependence Symptoms. AUDIT items 4 through 6 examine adverse reactions as a result of one's personal drinking behaviors/practices. More specifically, these items assess impaired control over drinking behaviors; that is, inability to cease drinking once started (Question 4), failure to perform normal expectations due to drinking (Question 5), and alcohol consumption the morning following a heavy drinking session (Question 6).

Harmful Alcohol Use. The final four items of the AUDIT examine harmful alcohol use. *Harmful* drinking is defined by the *presence* of physical and/or psychological consequences (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001). Therefore, this section assesses alcohol-related problems by exploring feelings of guilt or remorse after drinking within the past year (Question 7), blackouts (the inability to remember all events that transpired during the previous drinking session) experienced within the past year (Question 8), injuries to oneself or others as a result of drinking (Question 9), and whether others—friends, relatives, health professionals—express concern about one's drinking (Question 10).

SCORING AND INTERPRETATION

Each of the 10 items of the AUDIT is scored from 0 to 4, depending upon the respective response. Therefore, possible total scores range from 0 to 40 (Saunders, Aasland, Babor, De La Fuente, & Grant, 1993). The following table outlines the response scale for each of the 10 items and also designates the point value associated with each response.

Total AUDIT score typically denotes one's alcohol-related risk. Consequently, a higher total score corresponds to increased likelihood of hazardous and harmful drinking behavior. In general, total scores of 8 or greater are indicative of

hazardous and harmful alcohol use and may represent potential alcohol dependence. Due to individual characteristics, such as gender and body size, that influence the effects of alcohol, using a cut-off score of 7 is recommended to increase AUDIT sensitivity among populations of women and men older than 65 years of age. Conversely, using a criterion score of 10 increases the survey's specificity, and yet causes a loss of sensitivity (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001). In comparing AUDIT scores to diagnostic data relating to alcohol dependence, medium-level alcohol problems are represented by scores ranging from 8 to 15, whereas high-level alcohol problems are represented by scores of 16 or more (Miller, Zweben, DiClemente, & Rychtarik, 1992). Moreover, tentative guidelines suggest that scores between 8 and 15 typically require professionals to provide guidance addressing the reduction of hazardous drinking, while scores between 16 and 19 mandate brief counseling and further observation. AUDIT scores of 20 or greater merit further, in-depth alcohol dependence evaluation and may require referral to a specialist (Babor, Higgins-Biddle, Saunders, & Monteiro, 2001).

See also **Addiction: Concepts and Definitions; Alcoholism: Origin of the Term; Australia; Kenya; Mexico; Nordic Countries (Denmark, Finland, Iceland, Norway and Sweden); Research: Clinical Research.**

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ADAM E. BARRY

ALCOHOLICS ANONYMOUS.

Addiction to alcohol and other substances is arguably the greatest public health problem in the developed world. Societies have developed myriad ways to try to combat this complex problem. One of these ways, created by those who have personally experienced addiction, is an organization called Alcoholics Anonymous (AA). This entry provides an overview of AA, beginning with a definition of the organization, followed by a description of how it came into being and how it has evolved over the years. The core philosophy of AA is summarized, coupled with a description of the membership process and how affiliation works to promote recovery. Finally, scientific findings are brought to bear on the efficacy of AA compared to other treatments.

DEFINITION

AA is a mutual-help organization. Mutual-help organizations consist of persons voluntarily coming together with a shared problem and seeking solutions through the collective expression of their personal narratives (Humphreys, 2004). In the case of AA, that shared problem is addiction to alcohol. AA is self-directed and self-governed and does not rely on the expertise of any outside group or individual. The individual members themselves are in charge of the organization and provide expertise derived from their own lived experiences. Every member is both a provider and a recipient of help. This culture of reciprocal helping is at the very heart of AA and reflects the philosophy that even the most troubled people have the capacity to help others and that to help others is to help oneself (Maton, 1988). Other important features of AA include the absence of fees, the ubiquity of meetings, and a well-delineated program for change.

The absence of fees in AA is a practice that reduces potential barriers to participation. Individuals

with a broad spectrum of financial resources and levels of personal organization are involved (Humphreys & Tucker, 2002). The only criterion for attending an AA meeting is the desire to stop drinking alcohol. To pay for expenses such as coffee, room rental, and organizational literature, participants voluntarily contribute small amounts of money during meeting time.

The sheer number and ubiquity of AA meetings, found at all times of the day, all over the world, also greatly facilitates participation. Attendance need not be predicated on a specific time of day or location. Participation need not be discontinued if a member relocates to a new town. By breaking down financial and logistical barriers, AA provides a worldwide community that transcends time or place, offering nearly universal access to individuals who find themselves in chaos due to their alcoholism.

AA, unlike some other mutual-help organizations, has a developed philosophy and program of change outlined in a book titled *Alcoholics Anonymous*. The book was published in 1939 and is known universally by its members as *The Big Book* because of the thick paper on which it was originally printed (Humphreys, 2004). AA is not affiliated with any specific religion but does espouse the importance of spirituality and a Higher Power in the process of transformative healing.

ORIGINS AND DEVELOPMENT

AA was founded in 1935. Its origins can be traced to a 1920s American evangelical movement called the Oxford Group (Humphreys, 2004). The Oxford Group preached overcoming alcoholism through a spiritual transformation. Members of the Oxford Group who were struggling with alcoholism reached out to William Griffith Wilson (known as Bill W., the cofounder of AA). Wilson was an alcoholic who had tried repeatedly to stay sober. Members of the Oxford Group were ultimately able to convince Wilson that a spiritual transformation was indeed a key component of recovery. Wilson described his transformation, which occurred during yet another emergency detoxification, as follows: "the result was instant, electric, beyond description. The place lit up, blinding white .... Blazing came the tremendous thought: You are a free man" (W. 1949, p. 372).

In May 1935, through his Oxford Group connections, Wilson met with Dr. Robert Holbrook Smith (subsequently known as AA cofounder Dr. Bob), who also suffered from alcoholism for many years. The two men met and talked for several hours, and the first AA meeting was born. They both experienced a profound sense of healing in sharing their stories, and both came to believe that for alcoholics to recover, they need to meet and talk with other alcoholics. As Wilson wrote, "to talk with another alcoholic, even though I failed with him, was better than to do nothing" (Trice & Staudenmeier, 1989, p. 17). Smith was, in effect, Wilson's first sponsor.

Soon after, the two began working together with other alcoholics. By August 1936, AA meetings within an Oxford Group context were being held both in Akron, Ohio, and New York City. Both men decided to sever their relationship with the Oxford Group, primarily to move the organization out of a strictly Protestant religious framework that limited the appeal of AA to many alcoholics. The small AA groups were then on their own. By 1940, their newly formed board of trustees listed twenty-two cities in which groups were well established and holding weekly meetings. When the first edition of *The Big Book* was distributed (1939), AA had several hundred members. When Smith died in 1950, AA had 50,000 members. After 1950 AA steadily expanded and inspired similar organizations such as Narcotics Anonymous, Gamblers Anonymous, and Overeaters Anonymous. In the early twenty-first century, AA could be found in one hundred nations in addition to the United States and had perhaps five to six million members worldwide (Humphreys, 2004).

The incredible expansion of AA has necessitated a flexible organizational structure to provide cohesion and communication, without sacrificing the important AA precepts of autonomy and self-governance. Two coordinating groups have acted to link together the thousands of AA local groups in the United States and abroad. In the first year of AA, the founders, along with members of the first New York City group, formed a tax-free charitable trust with a board of trustees composed of both alcoholic and nonalcoholic members. It acted as a mechanism for the collection and management of

An Alcoholics Anonymous meeting. HANK MORGAN/PHOTO RESEARCHERS, INC.

voluntary contributions and as a general repository of the collective experience of all AA groups.

As of the early twenty-first century the board of trustees consists of fourteen alcoholic and seven nonalcoholic members who meet quarterly. At an annual conference, specific regions elect the alcoholic board members for four-year terms. The board appoints the nonalcoholic members for a maximum of three terms of three years each. An annual conference was established in 1955 at the Twentieth Anniversary Convention of AA. It expresses to the trustees the opinions and experiences of AA groups throughout the movement. Individuals in the General Service Office (GSO) in New York City interpret and implement the deliberations of these two groups on a daily basis.

PHILOSOPHY AND PROGRAM OF ALCOHOLICS ANONYMOUS

In AA, alcoholism is viewed as a disease with physical, moral, and spiritual components. The disease is conceptualized as a chronic one, from which one is never cured, but from which one can be in recovery by practicing the principles of AA. The core principles of AA are known as the *Twelve Steps*, and practicing them is called *working the program*. Full sobriety is achieved when the individual is abstinent from alcohol and working the program, which loosely summarized consists of living out the ideals of honesty, humility, selflessness, and mindfulness, in relationship with a Higher Power and others in one's community. Although the achievement of abstinence alone is considered important, it is not considered complete recovery in itself (Humphreys, 2004).

The idea of a spiritual transformation is a core feature of the early origins of AA, as well as a cornerstone of its philosophy. The Higher Power of AA is conceptualized or defined individually by group participants. Members may subscribe to any of various characterizations of God as a power beyond themselves, for example, a personal figure

such as Jesus Christ, the Christian concept of God, the ineffable mystery of the universe, or the awe-inspiring support and acceptance experienced through the community of AA fellowship. What is essential to the AA philosophy is not how members conceptualize the Higher Power, but rather that they are willing to give themselves over to that Higher Power, no longer relying exclusively on personal resources or ego for the answer to problems.

The spiritual aspect of AA can present an obstacle to participation for some would-be members. The use of the word *God* and *Higher Power* throughout the AA literature can be alienating for some persons who do not identify with such religious concepts. For these individuals, in particular, it is essential to point out that how one defines a power that lies beyond the self is individual and private, and it is not imposed by the organization. For this reason, the group emphasis on a power beyond the self need not prevent nonreligious individuals from becoming members (Humphreys, 2004).

AA asserts that in the disease of alcoholism, stopping drinking altogether, that is, total abstinence, is the core feature of recovery and that there is no place for drinking in moderation if one is an alcoholic. In the scientific literature, the outcome of abstinence versus moderate drinking not surprisingly appears to depend on the severity of physical dependence (Rosenberg, 1993). Having made the claim for abstinence, AA asserts that stopping the consumption of alcohol is necessary but not sufficient for full recovery. A *dry drunk* is an individual who is not drinking but who continues the behaviors typical of an alcoholic. Such individuals do not typically practice the steps that would lead to a spiritual transformation, and thus the chronic problems in their lives continue even though consumption of alcohol has ceased.

The AA program or path to sobriety is the Twelve Steps. They are as follows:

1. We admitted we were powerless over alcohol—that our lives had become unmanageable.
2. Came to believe that a Power greater than ourselves could restore us to sanity.
3. Made a decision to turn our will and our lives over to the care of God as we understood Him.
4. Made a searching and fearless moral inventory of ourselves.
5. Admitted to God, to ourselves, and to another human being the exact nature of our wrongs.
6. Were entirely ready to have God remove all these defects of character.
7. Humbly asked Him to remove our shortcomings.
8. Made a list of all persons we had harmed, and became willing to make amends to them all.
9. Made direct amends to such people wherever possible, except when to do so would injure them or others.
10. Continued to take personal inventory and when we were wrong promptly admitted it.
11. Sought through prayer and meditation to improve our conscious contact with God as we understood Him, praying only for knowledge of His will for us and power to carry that out.
12. Having had a spiritual awakening as the result of these steps, we tried to carry this message to alcoholics and to practice these principles in all our affairs.

PROCESS OF AFFILIATION

Affiliation is a process, not a single event within AA. Its elements and phases act to select and make ready certain alcoholics and problem drinkers for affiliation, leaving behind others with less readiness. The process begins before the problem drinker ever goes to a meeting (Trice, 1957). If the person has heard favorable reports about AA; if long-time drinking friendships have faded; if no will-power models of self-quitting have existed in the immediate background; and if the drinker has formed a habit of often sharing troubles with others, the stage is set for affiliation. It is further enhanced if, upon first attending meetings, the person has had experiences leading to the decision that the troubles associated with drinking far outweigh the pleasures of drinking (which is called *hitting bottom*). Typically, this means that affiliates, by contrasted with nonaffiliates, have had a longer and more severe history of alcoholism, and those with more severe alcohol problems are more likely to make consistent efforts to affiliate than are those with less severe problems (Emrick et al., 1993; Trice & Wahl, 1958).

Five other specific phases follow from those forces that make for commitment to the AA program: (1) first-stepping, (2) making a commitment, (3) accepting one's problem, (4) telling one's story, and (5) doing twelfth-step work (Rudy, 1986). First-stepping involves the initial contact with AA; it often entails orientation meetings that dwell on the group's notions of alcoholism as a disease and on step one in the twelve-step program: "We admitted we were powerless over alcohol . . . that our lives had become unmanageable." The newcomer in time may become associated with an experienced AA member, who may become the newcomer's sponsor. Quick action by the AA group—closeness of initial contact—to include the newcomer increases the likelihood of affiliation (Sonnenstuhl & Trice, 1987). Obviously interested newcomers are urged to take on the challenge of attending ninety meetings in ninety days. In effect, the receiving group seeks to keep a close watch over the newcomer, gently guiding the person to forego other commitments and increase commitments to the AA program.

Decisive third and fourth phases involve the willingness to tell one's own drinking story, with the beginning phrase, for example, "I'm Chris and I'm an alcoholic." Throughout the initial weeks and months, newcomers are gently and sometimes bluntly pressed to realize that they are alcoholics. They are encouraged to go public and tell their stories before the entire group at an open meeting. In numerous instances, newcomers may already have decided that they are alcoholic. In other cases, this realization may require a lengthy process of self-examination before it occurs. In still others, it may never occur, making them less likely to become authentic AA members. The public telling of one's story is an act of self-disclosure and ownership that conveys an inner conversion and acceptance of the precepts of AA. Members counsel newcomers on the appropriate first time to tell their stories, and their narrations are cause for many congratulations. Much applause typically attends this open act of commitment.

A final phase involves the literal execution of the program's twelfth step: "Having had a spiritual awakening as a result of these Steps, we tried to carry this message to alcoholics, and to practice these principles in all our affairs." In essence, doing twelfth-step work exemplifies a basic belief in AA, namely, one is never recovered from the disease; one is only recovering. As a consequence, a member can maintain sobriety only by remaining active in AA and by steadily engaging in carrying the program to those who are still active alcoholics. In short, by doing twelfth-step work, members reinforce their membership and the new definition of self.

Throughout this affiliation process, another dynamic can also be at work—slipping—a relapse into drinking by a recovering AA member. After reviewing six relevant studies, plus a summary of his own fieldwork with AA, Rudy reported that among both newly committed and longer-term members "slipping is a common occurrence, but it is possible that it serves a function in Alcoholics Anonymous. . . . [It is] a deviant behavior and the function of this deviance is boundary maintenance" (Rudy, 1980, p. 728). The response of most AA members to another's slipping is sympathy and understanding, sentiments that in turn enhance group solidarity. In essence, "their abstinence is dependent on interaction with those who slip" (Rudy, 1980, p. 731).

WHO AFFILIATES

What are the characteristics of people with drinking problems who undergo the affiliation process, contrasted with those who do not, even though exposed to the opportunity? Research in North America has consistently found no relationship between AA affiliation and demographic variables such as age, social class, race, employment status, and parental socio-economic status (Emrick et al., 1993; Trice & Roman, 1970). The fact that AA appeals to an extremely broad range of cultural, religious, and ethnic populations has been demonstrated by its adoption in cultures as diverse as Egypt, Brazil, Canada, India, Cameroon, Trinidad, and Japan, to cite only seven of more than one hundred nations in which the fellowship has taken hold (Humphreys, 2004).

Although it was once believed that AA affiliates have certain personality traits in common (Ogborne, 1989), this premise has not been demonstrated empirically. All that can be said confidently of research in this area is that sociability and comfort with group activities usually predict

greater AA affiliation, and discomfort with spiritual/religious topics usually predicts less affiliation. Yet even these generalities deserve qualification, as Internet-based meetings as of 2008 offered AA affiliation without group meetings, and many self-proclaimed atheists are AA (Mäkelä et al., 1996; Winzelberg & Humphreys, 1999).

In contrast, alcohol-problem characteristics have fairly consistently been shown to predict AA participation. In general, participation in AA is more likely when an individual's drinking problem is severe, as indexed by symptoms of physical dependence, intense anxiety about and loss of control over consumption, and high volume bingeing (Emrick et al., 1993). Greater problem severity predicts help-seeking of all forms (i.e., not just AA, but also treatment). A heavy drinker is more likely to recognize the existence of a problem, and other people are more likely to express worry and urge the drinker to take steps to change. But AA also tends to appeal to more seriously alcoholic individuals because that is the population its approach and philosophy are designed to help. The common AA stories of compulsive drinking, physical dependence, and hitting bottom heard in meetings and found in *The Big Book* reflect the experiences of the organization's founders and make its fellowship a particularly good fit for individuals whose lives have been negatively shaped by alcohol use. In contrast, some less severe problem drinkers find that the AA emphasis on loss of control, life calamities caused by drinking, and the need for lifelong abstinence are alien and off-putting (Klaw & Humphreys, 2000).

THERAPEUTIC MECHANISM

AA provides a new orientation, toward alcohol, toward oneself, and toward others. "One of A.A.'s great strengths lies in the quality of its social environment: the empathetic understanding, the acceptance and concern which alcoholics experience there which, along with other qualities, make it easier to internalize new ways of feeling, thinking, and doing" (Maxwell, 1982). Even brief exposure to AA introduces the alcoholic to the idea that self-regulation seems to be rarely achieved solely by self-reliance and willpower. Its basic premise describes the compelling sense of ego powerlessness, but it immediately offers the potent substitute of a viable community that provides individual attention, an explanation of alcoholism, and simple prescriptions for sobriety. "In a community that shares the same distresses and losses, accepts its members' vulnerabilities and applauds and rewards successes, A.A. provides a stabilizing, sustaining, and ultimately, transforming group experience" (Khantzian & Mack, 1989, p. 76).

Within the AA community, there are group-based specific therapeutic strategies unlikely to exist in professionally directed psychotherapy. Examples include (1) empirically based hope; (2) direct attack on denials; (3) practical guidelines for achieving sobriety; and (4) one-to-one sponsorship. When problem drinkers first attend meetings they are immediately aware of others who have confronted the same problem, and they hear these people speak about dramatic improvements in their lives through participation in AA and application of the twelve steps. Moreover, the AA program consistently reminds them that denial of the realities surrounding their drinking is a major barrier to any change. Telling one's story, either in open or closed sessions, helps to dissolve the entrenched denial that prevents positive change.

The twelve steps provide an organized approach for change and growing self-awareness. When members reach twelfth-step work, they see how much they have changed and how different they are from what they once had been, and this change reinforces their need to work the program. In addition, simple, practical guidelines are repeated in group-tested sayings that help people avoid using alcohol, such as first things first, one day at a time, and easy does it.

AA typically arranges for the informal sponsorship of newcomers, who often identify with and closely relate to their sponsors. Sponsors are recovering alcoholics who make themselves available at all hours of the day and night for phone or in-person discussion. Valuable treatment strategies are voluntary, free of charge, and occur between peers. Drinkers who drop out or who reject active membership in AA may nevertheless be helped by its unique therapeutic mechanisms. (Several organizations in the alcohol or drug recovery field use similar approaches.)

CRITICAL EVALUATIONS

AA existed for many years prior to much modern alcohol treatment research. As a result, it enjoyed a large membership and significant popular and

professional respect long before it was subjected to rigorous scientific evaluation. Some critics noted the lack of scientific demonstrations of AA's effectiveness as recently as the 1980s (Peele, 1989). However, in subsequent years, a number of longitudinal studies confirmed what AA members had long believed: AA involvement is a potent predictor of achieving and maintaining abstinence from alcohol (Emrick et al., 1993; Humphreys, 2004). AA participation also predicts improved psychological and social functioning (Humphreys, 2004).

Timko and her colleagues (2006), for example, randomized 345 substance abuse treatment outpatients to receive either a routine referral to AA and Narcotics Anonymous or an intensive referral in which clinical staff and peers actively facilitated involvement in the fellowship (Timko et al., 2006). At six-month follow-up, rates of twelve-step group involvement were substantially higher in the intensive referral condition, and improvement in drug and alcohol problems was 60 percent greater as well. This does not imply that AA alone is sufficient for all individuals with alcohol problems. In a well-known clinical trial, Walsh and colleagues (1991) showed that while assignment to AA alone produced significant reductions in drinking and related problems, even greater improvement was experienced by individuals who received AA supplemented by professional treatment (Walsh et al., 1991). As of the early twenty-first century, AA was extremely well respected in the addictions field by a wide range of treatment professionals.

One aspect of AA that continued as of 2008 to generate skepticism from some potential members and helping professionals is its spiritual emphasis. This issue has been a particularly sore one in the U.S. court system. Although AA is not a religion, it has sufficient spiritual content to convince a number of judges that mandating AA participation (for example, for drinking and driving offenders) violates the separation of church and state (Humphreys et al., 2004). Discomfort with AA's spiritual aspect has also led some individuals to create alternative organizations with different philosophies, including Smart Recovery and Secular Organization for Sobriety. For most members, however, AA's spiritual focus is sufficiently flexible and subjective that it accommodates personal beliefs, regardless of religious orientation or lack thereof.

AA is a mutual-help group for the alleviation of human suffering related to alcoholism and is potentially distinct from other treatments for alcoholism in that it relies on peer alcoholics helping each other through a specified program of change. AA meetings are free, occur at all times of the day, all over the world, and are open to anyone who has a genuine desire to stop drinking and heal their disease. AA began in the 1930s when two alcoholics (Bill W. and Dr. Bob) met and shared their personal narratives and through that encounter helped each other begin a process of recovery from their own addiction to alcohol. The two then resolved to go out and help other alcoholics in a similar way. From the 1930s into the twenty-first century, AA evolved into a worldwide organization with five to six million members. AA is not a religion, but it does espouse the importance of a spiritual transformation in the process of recovery. The exact mechanism through which AA helps alcoholics is not fully understood, but most certainly it includes the creation of a new social milieu, acceptance by people who have been there, constant reinforcement to work the program, not the least of which is seeing among beginning members how one's life used to look, and direct attack on denials by a group sophisticated in the many guises denial can take. Studies show that people from varied backgrounds have joined and benefited from membership in AA but that AA may ultimately be more accessible to individuals with more severe alcohol dependence. Longitudinal studies have confirmed the clear benefit of involvement in AA for achieving and maintaining abstinence, as well as improved social and psychological functioning.

See also **Alcoholism: Abstinence versus Controlled Drinking; Alcoholism: Origin of the Term; Gambling; Treatment: An Overview of Alcohol Abuse/Dependence.**

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ALCOHOLISM: ABSTINENCE VERSUS CONTROLLED DRINKING.

Until the 1970s therapists and researchers in the alcohol field accepted full and continuous abstinence as the only treatment goal for alcohol dependence. Every form of reduced use at the end of treatment was seen as complete failure and any renewed use after abstinence periods as a full relapse. This position became controversial when two young scientists published the results of a randomized clinical trial (Sobell & Sobell, 1973a, b) in which controlled drinking (CD) was not only observed but even supported as a treatment goal superior to traditional abstinence (not drinking [ND]). Amazingly, after 15 years of heavy debate and intensive research, the scientific community lost interest in this topic. Publications between 1985 and the early 2000s that attempted to clarify the mysteries of the debate were quite rare. Only a few empirical papers (e.g., Kavanagh et al., 1996; Heather et al., 2000; Dawson et al., 2005), some reviews and special

journal issues (e.g., Sobell & Sobell, 1995), and a series of commentaries; a detailed review by Klingemann and colleagues (2004) and a special issue in *Addiction Research & Theory* with contributions by Coldwell and Heather (2006) and others have targeted CD in those years.

This entry reviews the early studies and discusses relevant terms and concepts for CD as well as the scientific evidence. A final section offers conclusions for healthcare practice and research. According to modern classification (*DSM-IV-TR*, American Psychiatric Association, 2003) the entry uses *alcohol use disorder* (AUD) as a generic term for *alcohol abuse* and *alcohol dependence*, and *alcohol use problems* will cover a broader range, including also hazardous alcohol use (e.g., daily use of more than recommended quantities).

BACKGROUND AND HISTORY

The heated debate over this partly invidious controversy is hard to understand for those who did not experience this research period beginning in about 1985. At that time patients were mostly severe alcohol dependents, and abstinence was the only accepted treatment goal. In addition, and contrary to views held in Europe, the philosophy of Alcoholics Anonymous (AA) was the major theoretical backdrop for this treatment concept in the United States as well as the dominant political power determining the allocation of research funding, which hindered studies that questioned the traditional belief system.

After initial remarks in an earlier publication (Davies, Myers, & Sheperd, 1956), Davies (1962) published results of a follow-up study with treated alcohol dependents, between seven and eleven years after discharge. He found that seven out of 93 showed a normal alcohol use pattern. This paper caused an intensive European debate in journals (e.g., commentaries in the *Quarterly Journal Studies of Alcohol* in 1962) and conferences (for a description see Glatt, 1995). The heavy but controlled debate spilled over the other side of the Atlantic when two treatment studies were published from Australia (Lovibond & Caddy, 1970) and the United States (Sobell & Sobell, 1973a, 1973b, 1976). For the first time, controlled drinking was recognized as a preferred treatment goal, accompanied by a specific program to support this goal called *Individualized Behavior Therapy* (IBT). Components of IBT were, among others: functional analysis of the patients' drinking behavior (e.g., cues and reinforcement schedules), stress coping training, video confrontation with one's own (repulsive) behavior under the influence of alcohol and aversion therapy (in a bar situation, unwanted drinking behavior was punished by light electric stimulation). It is an irony that the Davies publication in 1962, which originally stimulated the debate on CD, was based on incorrect data about the drinking behavior of the seven patients (Edwards, 1985, 1994).

The design included two steps of treatment allocation (Sobell & Sobell, 1973a): 70 diagnosed male gamma-alcohol dependents according to the classification of Jellinek (1960), who had admitted themselves to treatment, were first assigned by the staff to either ND or CD. Patients were assigned on the basis of previous experiences with ND or CD, their personal preference, their belief in AA or CD principles, and the attitudes of their social support system. Then 50 percent of each group were randomly assigned to either an experimental or control condition. Each group received conventional state-hospital inpatient treatment: group discussions, participation in AA meetings, physiotherapy, and occupational therapy. The two experimental groups (ND- and CD-experimental) participated in 17 additional IBT sessions that took place in a bar and a living room-like laboratory setting (to establish real life conditions), with CD as goal in the CD groups and ND in the ND groups (Sobell & Sobell, 1973a). There is an inconsistency in the design description: According to Sobell and Sobell (1973b), the experimental groups did not receive the conventional treatment, in addition to IBT.

Follow-ups by the research group after one and two years analyzed the following: days of controlled alcohol use (maximum of six standard drinks daily), of full abstinence or relapse and days of "functioning well" (days of abstinence or CD), as well as a range of other outcome criteria (e.g., occupational, marital and driver's licence status, general outcome indices). A third year follow-up study was conducted by independent researchers who had no knowledge of the patients' treatment allocation (Caddy, Addington, & Perkins, 1978). The following results were found:

1. Subjects with the IBT program in the CD-setting (CD-E) had significantly more days of controlled alcohol use ("functioning well") than the controls (CD-C; 95% compared to 75% of the entire third year follow-up period);
2. CD-E had significantly fewer "drunk days" than CD-C, no differences were found for abstinent and CD days;
3. the "General Index of Outcome" was significantly better for CD-E than CD-C;
4. the IBT conditions (CD-E and ND-E) showed better outcomes in the vocational status than the controls. All reported significant differences between the CD groups that were not found between the two ND groups.

The results were quite stable over time and can be interpreted as follows:

1. IBT improves the combined rate of days with abstinence or controlled use ("functioning well") for patients with less severe alcohol use problems (CD conditions) compared to traditional treatment.
2. Patients with more severe problems (ND conditions) show a lower rate of "functioning well" days of alcohol use. This rate was not improved by IBT in comparison to traditional intervention.

Critics followed three lines of argumentation:

1. Based on the observation that the patients of the CD groups showed less severe alcohol use problems, the successful cases of CD were not seen as real *alcoholics.*
2. Others criticized the publication of the study because it might initiate an epidemic of relapse. The third critique by Pendery, Maltzman, and West (1982) accused the authors of having committed fraud, based on some questionable follow-up findings. This accusation heated up the controversy on the whole concept and conclusions, but was disproved later on by an independent committee (Dickens et al., 1982).

The background for the clash between the new concept and the dominant treatment philosophy at that time was a controversy about the degree of irreversibility of the problem behavior. "Loss of control" (Jellinek, 1960) was seen as the core symptom and as an unchangeable, biologically based incapacity of the alcohol dependent. This viewpoint was supported by the AA movement and the treatment professionals. But it was questioned by two young psychologists who argued that alcohol dependence should not be seen as an irreversible disease state, but as a learned negative behavior pattern that could be relearned with application of behavior therapy techniques just like any other human behavior. (For a discussion of the resulting scientific and popular controversy, see Marlatt, 1983). The controversy played out on several levels: between traditional concepts and new models for the understanding of AUD, between longstanding experience and new scientific evidence, between psychiatrists/counsellors and psychologists, between old and young.

PARALLEL AND SUBSEQUENT SCIENTIFIC DEVELOPMENTS

CD began to lose its explosive force around 1985. Emerging scientific evidence fundamentally changed major views on the alcohol problem and its treatment:

1. Progress in epidemiology: Increasing epidemiological research since 1970 and a better observation and measurement of alcohol use have shown that a wide range of patterns and intensities of alcohol use problems and different relapse patterns exist (Miller, 1996).
2. Development of a public health view: The increasing knowledge on the amount and range of AUD in the general population has stimulated a broader public health view on alcohol problems and the question of how to reduce the alcohol-related burden of a country. It became obvious for preventive purposes to also reach the much larger group of problem drinkers who did not show signs of physical dependence (tolerance and withdrawal). Therefore further CD research concentrated on this new group, combining the CD treatment goal with new interventions such as cognitive behavior therapy (CBT), motivational interviewing (MI), and brief interventions (stimulated by first papers from Orford, Oppenheimer, & Edwards, 1976, and Miller & Joyce, 1979; for an overview see Bien, Miller, & Tonigan, 1993; Miller, Wilbourne, & Hettema, 2003).
3. Refinement of treatment designs and outcome measures: Progress in better controlled

experimental designs (e.g., Project Match, 1993), better classification of patients (e.g., *DSM-IV*), and better questionnaires for the full range of alcohol-related problems (e.g., the AUDIT-Alcohol Use Disorder Identification Test, Saunders et al., 1993) reduced the critique on methodological weaknesses of the early treatment studies.

SCIENTIFIC EVIDENCE FOR CD

Later data from the U.S. National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, Dawson et al., 2005) reported 17.7 percent "low risk drinkers," and Vaillant (2003) found figures between 4 percent and 17 percent for "controlled drinking" (depending on the type of subcohort) in his 60-year longitudinal study. Treatment follow-up studies reported figures for CD in groups of "alcoholics" around 34 percent and in problem drinkers around 63 percent (Vogler, Weissbach, & Compton, 1977), 17 percent in groups with more or less severity of alcohol dependence (Heather et al., 2000), and 12 percent in alcohol dependents with ND treatments (Bottlender & Soyka, 2005; Polich, Armor, & Braiker, 1981). Altogether positive CD figures vary extremely between 5 percent and 90 percent (Körkel, 2002)!

Rosenberg (2004) summarized the patient and disorder characteristics that are found to be correlated with stable controlled drinking, either in ND or CD programs.

Severity of the dependence syndrome: One of the ongoing problems (Stockwell, 1986) and a topic of highly controversial debates remains the question if severity of AUD matters or not (Saunders et al., 1993). Both sides have some empirical support. Walters (2000) found in a meta-analysis of 17 CD trials that outcome is neither related to the severity of alcohol disorders nor to the type of *DSM* diagnosis. Miller and colleagues (1992) in a long-term follow-up study, Miller and Hester (1986) in a review, and Rosenberg (2004) concluded the contrary that dimensional measures of severity and dependence "reliably separated successful abstainers from successful asymptomatic drinkers" (Miller, 1992). Sanchez-Craig and Lei (1986) found that in a group of behavior problem drinkers, CD is superior to the AB treatment goal. There is some evidence that patients with less severe symptoms have a higher probability for successful CD. But there is no evidence-based cut-off point available as of 2008 for the allocation of patients to either CD or AB.

Self-concept/self-efficacy and alcohol belief system: Subjects who reject "being an alcoholic," which is probably related to less experience of tolerance, withdrawal, and other severe negative consequences, who have a positive attitude towards CD (Orford & Keddie, 1986) or a high self-concept to control alcohol use (Kavanagh, Sitharthan, & Sayer, 1996) tend to have a better outcome in CD.

Drinker's choice of the treatment goal: Several studies have shown that positive CD outcomes can be increased by following the problem drinkers' choice of treatment and treatment target (Booth et al., 1992). If more severe alcohol dependents are involved, the majority tends to choose ND at the beginning of treatment or change later on to ND (Öjehagen & Berglund, 1989; Hodgins et al., 1997).

Social support: The degree of positive social support, such as the drinker's social network or family attitudes and willingness to support, are also correlated with better outcome (e.g., Moos, Finney & Cronkite, 1990).

One might expect, that after 45 years of research into CD, specific treatment components would have been developed and tested improving the rate of successfully treated patients with CD. But there is consensus among most of the researches involved in the field, and supported by many studies, reviews, and meta-analyses (e.g., Walters, 2000; Heather et al., 2000), that there is no specific intervention and no specific treatment target that leads to a significantly higher rate of CD.

REFLECTING ON THE CONTROLLED DRINKING CONTROVERSY

In an invited editorial for the journal *Addiction*, Sobell and Sobell (1995) drew three conclusions

Dimensions of CD	Characteristics of ideal CD	Examples of positive CD outcome
(1) Low risk amount of daily use	Abstinence or < 20 g pure alcohol/day/(f.) < 30 g pure alcohol/day/(m.)	Continuous abstinence or ≤ 4 days/month with higher use than 20/30 g.
(2) No binge drinking	Less than 4 (f) or 5 (m) drinks in a drinking situation	≤ 4 binges/month
(3) Situational full abstinence • traffic • workplace • hazardous sport • pregnancy/breast feeding • certain diseases • use of certain medication	Abstinence in all critical situations	≤ 4 occasions of alcohol use/month in critical situations
(4) No functional use • for sedation and stress reduction • to overcome social inhibition	No functional use in critical situations Alternative behavioral repertoire	Functional use in <10% of critical situations/month Alternative coping skills

Table 1. Dimensions of and criteria for ideal CD for subjects with AUD and examples of criteria for positive outcome. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

from the research in the previous 25 years which remain valid in the early 2000s:

1. Recovery of severe alcohol dependents involves predominantly ND.
2. Recovery of problem drinkers involves predominantly CD (they called it "reduced drinking").
3. The prevalence and pattern of CD seem to be independent of the selected treatment program content and goal.

After 40 years of research on CD the following key lessons have been learned (for recent overviews, see also Booth, 2006; Heather, 2006). First, contrary to AA and early scientific belief CD does occur, even in the groups of alcohol dependents, but more prevalent in alcohol abusers, with or without formal intervention and with CD or ND as treatment goal. Second, CD figures cannot be increased systematically, either by specific intervention components, the type of treatment goal (ND or CD), or by treatment allocation guidelines, based on patient or disorder characteristics. These conclusions are an intriguing challenge to researchers' understanding of the core components and mechanisms of dependence, but quite disappointing for clinical practice. The difficulty of handling CD in clinical practice might partly explain large differences in the acceptance of CD: According to Rosenberg (2004), support for this treatment concept is widespread in Australia, Great Britain, and Scandinavia, whereas ND is the dominant approach in Northern America and Central and Western Europe.

CLARIFYING TERMS AND CONCEPTS FOR CONTROLLED DRINKING

Normal drinking, *social drinking*, *non-problem drinking*, *controlled drinking*, *reduced drinking*, *light and moderate drinking* are terms used to describe unproblematic alcohol use patterns beyond total abstinence (for details see Sobell & Sobell, 2004). This confusion is probably caused by a lack of clarity in defining and separating topics such as diagnoses (Babor & Caetano, 2008), treatment goals, treatment outcome criteria, or outcome measurement. Therefore, a core standard concept for CD is needed: From a public health view a pattern of low-risk use in terms of amount, pattern, situation, and drinking function should be the overall target for the whole (alcohol using) adult population, and also for CD of subjects with AUD. More specifically, this outcome would mean the following:

1. Less than about 30 g (m) resp. 20 g (f) pure alcohol/day (British Medical Association, 1995),

2. no binge drinking,
3. no alcohol use in critical situations like: workplace, dangerous sports, traffic, pregnancy, certain illnesses and use of certain medication,
4. no functional use to cope with stress, mood problems, or social deficits.

For historic and practical reasons researchers continue to use the term CD, but in the understanding and meaning of a low-risk alcohol use pattern. Table 1 depicts on the left side the mentioned dimensions of CD, in the center criteria for an ideal CD behavior, and on the right side examples for the definition of successful CD behavior in patient or population cohort studies. Such a concept could help to clarify CD behavior, and it enhances comparisons between different studies and allows comparable ratings of clinically relevant treatment progress.

IMPLICATIONS OF CONTROLLED DRINKING FOR CLINICAL PRACTICE

No sound evidence-based patient or disorders characteristics of successful CD have been detected as of 2008. Who is a candidate for CD? Clinical decisions should be guided by answers to the following questions:

1. Does the patient have a CD treatment goal preference and does he or she clearly believe in his or her abilities to cope with the demands of CD?
2. If yes,
3. Do patient and disorder characteristics enhance the probability for CD?
4. Do the somatic status and social/professional conditions allow CD?
5. Does a social support and control system exist for CD?
6. If all yes,
7. Do I as a therapist accept and support CD, and am I able to treat the patient adequately?

To be more on the safe side in therapeutic decision-making, it is recommended that only those patients be selected who have a higher chance for stable CD. Doing so would exclude patients with a more severe load of symptoms, more negative social conditions, a history of continued relapse, individuals with alcohol-related somatic disorders, and any patient with specific professional conditions that require full abstinence (e.g., pilots).

The decision process becomes even more complicated for deprived patients with longstanding and severe AUD, where abstinence is the only reasonable treatment choice, but is not accepted as a goal by patients. In these cases, is controlled use less harmful than uncontrolled use? There is no evidence as of 2008 for correct procedures, but an ethical requirement to also help those patients. Pros and cons have to be weighed carefully. Therapists have to base their decisions on personal experience and probably on a *stepped-care* procedure (Sobell & Sobell, 2000).

Heather (2006) distinguishes three target groups for CD:

1. Non-treatment seeking subjects with alcohol use problems: This group covers the hazardous/harmful alcohol users and those with *DSM-IV* abuse. They are either targeted by population-based preventive guidelines to control their drinking pattern or by early screening in the general medical services.
2. Subjects with alcohol use disorders seeking treatment: This group of patients can be found in outpatient and inpatient treatment centers and usually have at least a dependence diagnosis, with signs of a more severe state of dependence.
3. Subjects with severe alcohol use disorders and high comorbidity not motivated for treatment: This group is characterized by severe patterns of alcohol dependence, long history, high comorbidity, and a high level of social problems (homeless, unemployed, living in an alcohol positive environment). In many cases it is highly unrealistic to attempt to motivate these patients for abstinence treatment, and any improvement in the amount and pattern of abuse might be helpful for their survival.

As of 2008, much remained unexplained about the controlled drinking controversy. A cooperative effort involving addiction research, experimental psychology, and cognitive neuroscience is urgently needed to shed light on this 40-year-old mystery.

See also **Alcohol.**

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ALCOHOLISM: ORIGIN OF THE TERM.

The term *alcoholism* is of relatively recent date; knowledge of the adverse effects of heavy alcohol

(ethanol) consumption is not. A proverb describes alcohol as "both mankind's oldest friend and oldest enemy." Alcohol occurs in nature, and humans have long known how to ferment plants to create it; both its moderate and excessive use have therefore occurred since prehistory. The Bible cautions: "Do not look at wine when it is red, when it sparkles in the cup and goes down smoothly. At the end it bites like a serpent and stings like an adder" (Proverbs 23:31–32). A drunken Noah (Genesis 9:20–28) is one of a long line of such literary descriptions. In the Greco-Roman era drunks appeared in the *Character Sketches* of Theophrastus, in the *Satyricon* of Petronius Arbiter, and in the *Epistles* of Seneca. Shakespeare's porter in *Macbeth* (Act II, Scene 3) was another.

EARLY HISTORY

Viewing the long-term adverse effects of alcohol as a disease predates the term *alcoholism*. Benjamin Rush (1745–1813) and Thomas Trotter (1760–1832), both physicians, wrote extensively in this vein, using words such as *drunkenness*. Their elder contemporary Benjamin Franklin (1706–1790) produced a glossary of 228 synonyms in use in 1737 for "being under the influence of alcohol." It was not until 1849 that the Swedish physician and temperance advocate Magnus Huss (1807–1890) first used the word *alcoholism* in his book *Alcoholismus Chronicus (The Chronic Alcohol-disease)*. Huss's term, used originally in a descriptive sense to denote the consequences of the prolonged consumption of large quantities of alcohol, has come to connote a disease, believed by some to result in such consumption.

Huss meant by the term *chronic alcoholism* "those pathologic symptoms which develop in such persons who over a long period of time continually use wine or other alcoholic beverages in large quantities" and stated that it "corresponds with chronic poisoning." His book is filled with detailed case histories illustrating the various symptoms that might occur. Sweden was at that time ranked highest in the list of countries that consumed liquors, and Huss, as attending physician to the Serafim Clinic in Stockholm, had ample opportunity to observe cases. The London *Daily News* of December 8, 1869, carried a story on "the deaths of two persons from alcoholism," which according to the *Oxford English Dictionary* was the first popular use of the word in English. From that time on, its use in both the professional and the popular literature greatly expanded.

TEMPERANCE MOVEMENT

In the United States during this period, the term *drunknness* was commonly used to refer to excessive use of alcohol. The Temperance Movement during the nineteenth and early twentieth centuries in America arose in response to increasing social and physiological difficulties attributed to drunkenness. With the growing use of distilled drinks in America, increased awareness was drawn to their effects when used to excess (domestic violence, decreased work performance, etc.). As a result, groups inspired by religious leaders advocating moderation in (temperance) or abstention from alcohol use came together in the Temperance Movement. Temperance Associations, many of them based in the New England states, formed in increasing numbers. At the zenith of the movement (1830s), there were more than 6,000 local Temperance organizations across the United States.

The Temperance movement was international. One of the first U. S. groups to cross the ocean was the Order of the Good Templars, formed in Utica, New York, in 1851. Among the most popular Temperance Groups in America were the Women's Christian Temperance Union (created in 1874) and the Anti-Saloon League (founded in 1895). Among the more well-known Temperance advocates were Carrie Nation, Susan B. Anthony, and Frances E. Willard. Some of the lasting effects of the women's temperance movement were the passage of legislation requiring government regulation of the import, manufacture, and sale of alcohol; impetus toward research on the long-term and chronic effects of alcohol use; and a mandate that alcohol education become part of the national academic curriculum for primary and secondary students.

As these factions gained in membership and power in America, they essentially became political activist groups and effectively lobbied for governmental control of liquor throughout the country. They were successful in the creation and passage of numerous pieces of legislation, one of which was the 18th Amendment authorizing prohibition.

PROHIBITION

During the period of national prohibition in the United States (1919–1933) little attention was

paid to the consequences of alcohol consumption. Because consumption was illegal—permanently, it was assumed—it was thought that there would be few consequences. Indeed, such consequences as cirrhosis of the liver did decline abruptly during this period. But as enthusiasm for prohibition waned, and especially after it was repealed, a need to promote treatment became increasingly evident. One group involved in this promotion used *alcoholism* as the key word in their efforts, and accordingly were called the *alcoholism movement* by sociologists who subsequently studied their work. In an early statement of this movement, Dwight Anderson (1942) predicted that "When the dissemination of these ideas is begun through the existing media of public information, press, radio, and platform, which will consider them as news, a new public attitude can be shaped." It was also felt that the term, together with the disease connotations attached to it, would encourage the involvement of physicians in its study and treatment. The medical profession was viewed as critical to the success of the effort to increase the nation's concern about the consequences of alcohol consumption. The formation in 1944 of the National Council on Alcoholism, the largest public interest group in this area, was a project of the same movement. Their successful efforts may be the reason that the term *alcoholism* developed and sustained a degree of popularity in the United States beyond that which it achieved in Europe or even in Scandinavia, where it was first used.

CENTER OF ALCOHOL STUDIES

During the late 1930s and 1940s, the Center of Alcohol Studies, the first interdisciplinary research center devoted exclusively to alcohol-related problems and issues, was developed. Initially located at Yale University, it was directed by physician Dr. Edward W. Haggard (Yale University Laboratory of Applied Physiology and Biodynamics) and also physiologist and biostatistician E. M. Jellinek. Jellinek headed the Section on Alcohol Studies, which focused on the effects of alcohol on the body. Dr. Haggard was also the founder in 1940 of the seminal publication titled the *Quarterly Journal of Studies on Alcohol.* The *Quarterly Journal of Studies on Alcohol* has evolved into the highly respected, juried *Journal of Studies on Alcohol.*

With the concept of alcoholism growing through Prohibition, there was an increased need for studying the subject, resulting in the creation of Yale's Summer School of Alcohol Studies in 1943. In 1944 Yale founded the Yale Pain Clinics, the first outpatient alcoholism treatment facilities in the nation.

The Yale Center of Alcohol Studies was at the forefront of the medical and sociocultural movement dedicated to the recognition of alcoholism as a major public health issue. As a result, in the 1950s the American Medical Association formally accepted alcoholism as a diagnosable and treatable illness.

In 1962 the Center relocated from Yale to Rutgers University. Subject matter experts from the Center are frequently called upon by the World Health Organization, the National States' Conference on Alcoholism, the Cooperative Commission on the Study of Alcoholism, and by the National Council on Alcoholism Blue Ribbon Panels. The Center is largely responsible for federal legislation that created the National Alcohol Research Center Program.

UNDERSTANDING OF ALCOHOLISM BROADENED

As the term *alcoholism* became widely used, its meaning broadened. In a 1941 review of treatment, ten definitions of chronic alcoholism and sixteen definitions of alcohol addiction were collected from the international literature. Originally used by Huss to refer to a disease that consisted of the *consequences* of alcohol consumption, *alcoholism* came in time to represent a disease that *caused* high levels of alcohol consumption (Jellinek, 1960). A variant theory attempts to preserve the original meaning: High levels of alcohol consumption resulted in damage to the central nervous system, which in turn caused the high levels of consumption to continue (Vaillant, 1983). That is, the term *alcoholism* evolved over time from a primarily descriptive term to a largely explanatory concept. An example of a definition of *alcoholism* with clear explanatory intent is one that Robert Rinaldi and colleagues produced in 1988 through an elaborate consensus exercise (a Delphi process) among eighty American experts, who defined the term as "a chronic, progressive, and potentially fatal biogenetic and psychosocial disease characterized by tolerance and physical dependence manifested by a loss of control, as well as diverse personality changes and social consequences" (Rinaldi et al., 1988). As a counterpoint to this development, a growing and increasingly influential literature holds that problems developing in the context of alcohol consumption do not constitute a disease at all (Fingarette, 1988).

The greater interest taken in alcohol consumption and its consequences as a result of the popularization of the term *alcoholism* has been both useful and problematic. For example, in a review of alternative definitions, Thomas Babor and Ronald Kadden (1985) concluded: "Clearly, the past and present lack of consensus concerning the definition of alcoholism and the criteria for its diagnosis does not provide a solid conceptual basis to design screening procedures for early detection or casefinding." Because of its imprecise meaning, the term *alcoholism* was now dropped from the two major official systems of diagnosis of diseases—the International Classification of Diseases of the World Health Organization and the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV-TR*) of the American Psychiatric Association—where it has been replaced by a variety of alcohol-use, alcohol-related, and alcohol-induced disorder terminologies. A recent comprehensive study of treatment deliberately avoided the use of the word *alcoholism*, but suggested that the word was not incompatible with the phrase that it chose to use—*alcohol problems*—to refer to any problem occurring in the context of alcohol consumption (Institute of Medicine, 1990, pp. 30–31).

COMPLEX PROBLEMS

Recent attempts to be precise represent a return to the more straightforward, descriptive use of *alcoholism* by its originator, Huss. Two major realities contributed to this change of direction. One is that the problems people experience from alcohol use are complex. Although alcohol may be a factor in some such problems—even an important factor—it is not often the full explanation for them. Multiple factors, including heredity, early environment, cultural factors, personality factors, situational factors, and others, contribute to the development of human problems and must be considered in their resolution. This formulation does not minimize the important role of alcohol in such problems or say that reducing or eliminating alcohol consumption may not be a critical factor in resolving them. Secondly, an extremely broad spectrum of problems arises in the context of alcohol consumption. Although a substantial proportion of these problems arise from those who drink too much over a long period of time and who usually have multiple problems (those to whom the term *alcoholism* is applied), an even greater burden of problems arises from those who drink too much over *short* periods of time and who have only a *few* problems. The simple reason is that there are more of the latter than of the former (Institute of Medicine, 1990, chapter 9). Effectively reducing the burden upon society requires dealing with both populations. An exclusive concentration on *alcoholism* may overlook this reality.

The term *alcoholism* retains its place in general, nontechnical speech as an indicator of serious problems that are the consequences of prolonged heavy alcohol consumption. Its continued popularity has some advantages, for the public-health consequences of such alcohol consumption are enormous. The presence of a convenient shorthand term for this fact in the public consciousness—*alcoholism*—serves as a continuing reminder of this major unfinished item on the public-health agenda. Certainly, there is a legitimate place in society for the use of alcohol. With equal certainty, too many individuals fail to use alcohol wisely or well.

COSTLY CONSEQUENCES

The ravages that prolonged exposure to alcohol produces in the human body are manifold, as Huss well understood. They include, but are not limited to, neurological problems (damage to the central and peripheral nervous systems), cirrhosis (fibrosis and shrinking) and other diseases of the liver, hypertension (high blood pressure), heart disease, psychological disorders, and many forms of cancer, particularly of the digestive tract. Added to these, consequences of short-term but intense exposure to alcohol also include the common behavioral effects of intoxication as well as a high proportion of all accidents, burns, violence, suicide, and especially automobile crashes.

The National Survey on Drug Use and Health (NSDUH) asks persons who are 12 or more years of age a variety of questions about alcohol use, abuse, and dependence during the past year, using *DSM-IV*-specified criteria such as symptoms of withdrawal, increased tolerance, use in dangerous situations, interactions with law enforcement and the legal system, and interference with major obligations and responsibilities such as school, job, or family. According to averages gleaned from surveys conducted in 2002, 2003, and 2004; 7.6 percent, or 18.2 million people, age 12 or older met clinical criteria for alcohol abuse or dependence. Broken out by age group, this corresponds to 5.9 percent

of those aged 12 to 17, 17.4 percent of those 18 to 25, 11.1 percent of 26 to 34 year olds, 7.5 percent aged 35 to 49, and 3.0 percent among those 50 or more years of age.

When looked at in terms of ethnicity, Native Americans or Alaskan Natives had the highest incidence of alcohol abuse or dependence (14.0%), followed by Native Hawaiians or Pacific Islanders (8.5%), Hispanics (8.2%), Caucasians (7.9%), African-Americans (6.5%), and Asians (4.3%). Poverty and alcohol abuse or dependence are statistically linked: 9.4 percent of persons with family incomes of less than 125 percent of the federal poverty threshold met abuse or dependence criteria. This decreased to 7.7 percent of those with family incomes between 125 percent and 199 percent of federal poverty threshold, fell to 7.2 percent of those with family incomes between 200 percent and 399 percent of the federal poverty threshold, and remained at 7.2 percent of those living at 400 percent or more of the federal poverty threshold. Individuals who met criteria for alcohol abuse or dependence were also more likely to have been treated at an emergency medical facility (ER or Urgent Care facility) than their non-alcohol abusing or dependent peers (34.2% and 27.9%, respectively).

The difficulties that alcohol abuse or dependence create are legion—and its remediation would be a remarkable step forward.

See also **Alcohol: History of Drinking in the United States; National Survey on Drug Use and Health (NSDUH); Prohibition of Alcohol; Temperance Movement; Woman's Christian Temperance Union.**

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ALKALOIDS. This is the general term for any number of complex organic bases that are found in nature in seed-bearing plants. These substances are usually colorless but bitter to the taste. Alkaloids often contain nitrogen and oxygen and possess important physiological properties.

Examples of alkaloids include not only quinine, atropine, and strychnine but also caffeine, nicotine, morphine, codeine, and cocaine. Therefore, many drugs that are used by humans for both medical and nonmedical purposes are produced in nature in the form of alkaloids. Naturally occurring receptors for many alkaloids have also been identified in humans and other animals, suggesting an evolutionary role for the alkaloids in physiological processes.

See also **Caffeine; Cocaine; Codeine; Morphine; Nicotine.**

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ALLERGIES TO ALCOHOL AND DRUGS. In addition to alcohol, opiates, and barbiturates, some street drugs have been reported to induce allergic reactions. These allergic phenomena are most frequently mediated by reactions of the immune system known as immediate hypersensitivity and delayed hypersensitivity. Immediate hypersensitivity is mediated by the serum protein immunoglobulin E (IgE), whereas delayed hypersensitivity is mediated by thymus-derived lymphocytes (the white blood cells called T cells).

IMMEDIATE HYPERSENSITIVITY

The symptoms and signs associated with IgE-mediated immune reactions are urticaria (hives); bronchospasm that produces wheezing; angioedema (swelling) of face and lips, or full-blown anaphylaxis (a combination of all the above symptoms and lowering of blood pressure). Abdominal pain and cardiac arrhythmias (irregular heartbeat) may also occur with anaphylaxis. Any or all of these symptoms occur when IgE, which has previously been synthesized by a sensitized lymphocyte, fixes to mast cells or basophils in the skin, bronchial mucosa, and intestinal mucosa. This cell-fixed IgE then binds the antigen that triggers the release of the following: histamine, slow-reacting substance of anaphylaxis (SRSA), bradykinin, and other mediators that induce these symptoms. Examples of this type of allergic reaction are the allergic responses to either bee stings or to penicillin.

Similar symptoms may also occur when mediators are released by mast cells in response to chemical or physical stimuli, which is called an anaphylactoid reaction. In this instance, the mast cell or basophil is directly activated by the chemical to release mediators without having to bind to IgE. Examples of this type of reaction are responses to intravenous contrast material, such as dye injected for diagnostic imaging procedures, or the hives induced by exposure to cold.

DELAYED HYPERSENSITIVITY

Reactions occur when antigenic chemicals stimulate T lymphocytes and induce their proliferation. T effector cells are then recruited into the tissue site. These effector cells bind the antigen and subsequently release effector molecules, such as interleukins, chemotactic factors, and enzymes. These effector molecules induce an inflammatory response in the area and may also induce formation of a granuloma (a mass of inflamed tissue) by macrophages and inflammatory cells. Symptoms of delayed hypersensitivity reactions are skin rashes, which may be red, pruritic (itchy), or bullous (blistered) in nature. Granulomas can cause lymph node enlargement and nodules in the skin or in organs. Examples of this response are poison ivy, cosmetic allergies, erythema nodosum, and sarcoidosis.

ALLERGIC RESPONSE TO ALCOHOL

True anaphylactic or anaphylactoid reactions to alcohol (ethanol) are rare. More commonly, people who report hives, facial flushing, nausea, tachycardia, or other reactions to alcohol are actually experiencing the so-called alcohol flushing reaction.

This reaction occurs most commonly in individuals who lack an active form of an enzyme, acetaldehyde dehydrogenase, which is essential to the metabolism of alcohol. People who have this condition complete the first step of alcohol metabolism, conversion of alcohol to acetaldehyde, a toxic intermediary, but are slow to complete the second step, conversion of acetaldehyde to acetate, a common waste product. The acetaldehyde builds up rapidly, causing the flushing reaction. The alcohol flushing reaction occurs most commonly among Asians; up to 40 percent carry the gene encoding the inactive enzyme, though the gene also occurs in other ethnic groups. Not unexpectedly, this genetic variation is associated with a decreased risk of alcoholism. It is a less severe reaction than that occurring when an individual ingests alcohol after having been treated with the medication disulfiram (Antabuse), which irreversibly blocks the enzyme acetaldehyde dehydrogenase. Symptoms of the disulfiram-ethanol reaction may include flushing, nausea, vomiting, shortness of breath, sweating, dizziness, blurred vision, and confusion.

Most true allergic reactions to ingested alcoholic beverages are actually secondary to other chemicals in the beverage such as yeasts, metabisulfite preservatives, papain, or dyes. However, there are reports of true allergic reactions in which the offending agent was shown to be ethanol itself. Symptoms of anaphylaxis have been reported to occur in several subjects following ingestion of beer and/or wine, and these symptoms were reproduced in one patient by administration of 95 percent ethanol. Hives have been reported with ethanol ingestion, and hives on contact with ethanol have been reported for some Asian patients. Bronchospasm was precipitated in some asthmatic patients by administration of ethanol, and contact hypersensitivity to 50 percent ethanol solution was produced in 6 percent of subjects tested.

ALLERGIES TO OPIATES, BARBITURATES, AND STREET DRUGS

There have been reports of morphine-induced hives in some people, and studies show that morphine can

cause histamine release directly from cells without binding to specific receptors on cells. Anaphylaxis may also occur with either morphine or codeine, and IgE antibodies against morphine and codeine have been found in patients experiencing anaphylaxis. Thus, the opiates can mediate allergic reaction by either mechanism, and the antagonist drug naloxone will not reverse these reactions. There are also reports of heroin causing bronchospasm.

Some instances of anaphylaxis associated with the medical administration of opiates or local anesthesia during surgery are due to the often-included preservative methylparaben, rather than to the opiate itself. Anaphylaxis may occur with more than one local anesthetic and/or analgesic compound in the same patient because of the methylparaben preservative. Numerous reports exist for anaphylactoid reactions following the use of barbiturates for the induction of anesthesia. The drugs themselves may induce histamine release. This may also be mediated through a true allergic IgE mediated response in some patients. Skin rashes also occur frequently following barbiturate usage, which may be a hypersensitivity reaction or a pseudo-allergic reaction.

Street drugs have been reported to induce asthma and/or anaphylaxis. Bronchospasm may occur in patients smoking cocaine or in those injecting heroin. This response may occur more often in patients who have a previous history of asthma. The asthma may persist after the subjects have stopped smoking cocaine. Pulmonary edema (fluid in the lungs) may also occur with freebasing cocaine.

These side effects are not likely to be mediated by the immune system. However, a hypersensitivity pneumonitis to cocaine has been described and is associated with elevated levels of IgE. Marijuana does not appear to increase the incidence of either asthma or anaphylaxis.

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AMANTADINE. Amantadine is a medication (Symmetrel) that is believed to be an indirect dopamine agonist; this means that it releases the neurotransmitter dopamine from nerve terminals in the brain. Since some of the symptoms of cocaine withdrawal and cocaine dependence are thought to be related to abnormalities in the dopamine systems of the brain, and these are thought to contribute to relapse, amantadine has been examined as a treatment possibility.

After chronic cocaine use, many patients' dopamine systems either fail to release sufficient dopamine or are insensitive to the dopamine that is released. This relative dopamine deficit is believed to be responsible for the dysphoria of cocaine withdrawal. It was hoped that amantadine would relieve their dysphoria and reduce

relapse back to cocaine abuse by increasing the release of dopamine in the brains of cocaine-dependent patients. Amantadine has been effective in reducing depressive symptoms in patients with neurological disorders such as Parkinson's disease, which is due to the death of dopamine-producing cells in the brain; however, no solid evidence exists that it is helpful in preventing continued cocaine use or relapse to cocaine use after detoxification.

See also **Cocaine; Treatment, Stages/Phases of: Medical Detoxification; Withdrawal: Cocaine.**

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AMERICAN SOCIETY OF ADDICTION MEDICINE (ASAM). The American Society of Addiction Medicine (4601 North Park Avenue, Arcade Suite 101, Chevy Chase, MD 20815; http://www.asam.org) is a not-for-profit organization of physicians in all medical specialties and subspecialties who devote a significant part of their practice to treating patients addicted to, or having problems with, alcohol, nicotine, and other drugs. The society strives to have addiction recognized as a medical disorder by health insurance and managed care providers, and the medical community at large. Many of its members are actively involved in medical education, research, and public policy issues concerning the treatment and prevention of addiction.

The roots of ASAM can be traced to the early 1950s, when Dr. Ruth Fox organized regular meetings at the New York Academy of Medicine with other physicians interested in alcoholism and its treatment. These meetings led to the establishment, in 1954, of the New York City Medical Society on Alcoholism, which eventually became the American Medical Society on Alcoholism (AMSA). Another state medical society devoted to addiction as a subspecialty, the California Society for the Treatment of Alcoholism and Other Drug Dependencies, was established in the 1970s. By 1982, the American Academy of Addictionology was incorporated, and all these groups united within AMSA the following year. Because the organization was concerned with all drugs of addiction, not only alcohol, and was interested in establishing addiction medicine as part of mainstream medical practice, the organization was renamed the American Society on Alcoholism and Other Drug Dependencies, which in 1989 was changed to the American Society of Addiction Medicine (ASAM). In 1988, the American Medical Association (AMA) House of Delegates admitted ASAM as a voting member, and in 1990, the AMA recognized addiction medicine as a medical specialty. In the late 1990s, ASAM and the American Managed Behavioral Healthcare Association (AMBHA) began an ongoing collaboration to publish statements of consensus on various issues such as the effective treatment of addictive disorders and credentialing of clinical professionals, among others. The stated mission and goals of ASAM are to increase access to and improve the quality of addictions treatment; educate physicians, medical students, and the public; promote research and prevention; and establish addiction medicine as a specialty recognized by the American Board of Medical Specialties.

By the early 2000s, membership in the society exceeded 2,500, with chapters in all fifty states, as well as overseas. Membership consists of private- and group-practice physicians, corporate medical directors, residents, and medical students, as well as retired physicians. ASAM-certified members with at least five years of active participation in the society, as well as involvement in related organizations and activities, may become Fellows.

Educational activities of the society are conducted through publications, courses, and clinical and scientific conferences. Publications include, among others, a bimonthly newsletter, *ASAM News*; the *Journal of Addictive Diseases*, published quarterly; the *ASAM Principles of Addiction Medicine*, a comprehensive reference guide; and the *Patient Placement Criteria for the Treatment of Substance–Related Disorders*, a clinical guide for matching adult and adolescent patients to appropriate levels of care. Courses include the Ruth Fox Course for Physicians; Medical Review Officer

(MRO) certification training; and in-depth studies of addiction medicine. An annual medical–scientific conference includes scientific symposia, clinically oriented courses and workshops, and presentations of submitted papers.

In April 2001, ASAM revised its Patient Placement Criteria for the Treatment of Substance-Related Disorders to make consistent diagnostic terminology with language within the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (*DSM–IV*). This revised edition was borne of numerous requests to ASAM for criteria that more effectively meet the needs of patients suffering from both mental and substance-related afflictions. In addition to reiterating and updating its guide for adult and adolescent levels of care, the revised edition addresses the concept of the *unbundling* of clinical services, which takes into account the needs of individual patients as opposed to the limitations of a particular treatment setting.

In its continued effort to establish the legitimacy of addiction medicine as a subspecialty within medicine, ASAM administers a six-hour certification examination, is a primary sponsor of medical postgraduate fellowships in alcoholism and drug abuse, and has developed guidelines for the training of physicians in this area of medical practice.

ASAM aggressively lobbies Congress on various mental health and substance-related health issues. After the U.S. Senate passed similar legislation in 2007, eighteen ASAM representatives visited members of Congress in support of HR 1424, also known as the *parity bill*, which would expand 1996 mental health legislation. HR 1424 would require group health plans to provide mental and/or substance abuse benefits at a level equal to medical and surgical benefits. A vote of the House of Representatives was expected in 2008. In addition to its personal lobbying efforts, the ASAM Web site offers a parity "War Room," instructing ASAM members on talking points, sample letters, and other strategies for influencing Congress, as well as distributing e-newsletters and other information to members.

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AMOBARBITAL. Amobarbital (Amytal) is one of the many different members of the barbiturate family of central nervous system depressants used to produce relaxation, sleep, anesthesia, and anticonvulsant effects. In terms of the duration of its effects, it is considered an intermediate-acting barbiturate. When taken by mouth, its sedating effects take about 1 hour to develop and last about 6 to 8 hours, although it takes considerably longer for all the drug to leave the body.

In addition to its use as a sedative, amobarbital is occasionally used in psychiatric evaluation in so-called Amytal interviews, to relax patients in order to help them recall memories or information that has been repressed due to trauma. This technique was sometimes called *narcoanalysis* or *narcotherapy.*

DOSAGE AND ADMINISTRATION

Amobarbital may be given orally, intramuscularly, or intravenously for the treatment of insomnia or anxiety. The adult dosage for sedation is 15 to 50 milligrams but 65 to 200 milligrams for sleep. For treating convulsions, the adult dose is 65 to 200 milligrams, with a maximum dose of 500 milligrams.

Amobarbital should not be given to patients with a history of addiction; personal or family history of porphyria; severe kidney, liver, or lung disease; or hypersensitivity to barbiturates.

Amobarbital is incompatible with a number of medications, including dimenhydrinate, phenytoin, hydrocortisone, insulin, morphine, cimetidine, pancuronium, streptomycin, tetracycline, vancomycin, and penicillin G. It may decrease the effectiveness of birth control pills containing estrogen. It has also

been shown to increase the risk of birth defects if taken during pregnancy.

PSYCHIATRIC USE

The use of amobarbital in "Amytal interviews" has declined since the mid-1990s because of its relatively low success rate. One medical text published in the mid-1990s noted that the amount of clinically useful information obtained by this method is quite limited. Amobarbital interviews appear to be useful primarily in distinguishing between psychosis and delirium. Psychotic patients usually improve with amobarbital, whereas delirious patients get worse.

DEPENDENCY AND ABUSE

Amobarbital has been largely replaced by benzodiazepine medications as a sedative because of the high risk of abuse. It has been dropped from the 1999 edition of the *Physicians' Desk Reference*, which implies that it is no longer manufactured in the United States. As of 2000, it is still available in Canada. Although amobarbital has been less popular with addicted patients than the more rapidly acting barbiturates (secobarbital and pentobarbital), it is still sold on the street as "blues" or "rainbows" (combinations of amobarbital and secobarbital). A daily dose of 500 to 600 milligrams is considered sufficient to produce dependence. The time necessary to produce dependence is estimated at 30 days. It has often been noted that the symptoms of barbiturate dependence resemble those of chronic alcoholism, though barbiturate withdrawl is more often associated with life-threatening complications than alcohol withdrawl.

EMERGENCY TREATMENT

Overdose. Although the toxic dose of amobarbital varies according to height, weight, and other factors, 1 gram taken by mouth usually produces serious poisoning in an adult. Two to 10 grams are usually a fatal dose. Emergency treatment is supportive, including oxygen administration if necessary, fluid therapy and other standard treatment for shock, and forced diuresis if the patient has normal kidney function. This procedure speeds the excretion of the barbiturate in the urine.

Withdrawal. The symptoms of withdrawal from amobarbital or any barbiturate may be severe or even fatal if the patient has been taking the drug in large doses (800 mg/day). The barbiturate withdrawal syndrome is similar to delirium tremens. Within 12 to 20 hours after withdrawal, the patient becomes restless and weak. During the second and third days, 75 percent of patients develop convulsions, which may progress to status epilepticus and death. From the third to the fifth day, untreated withdrawal syndrome is marked by delirium, hallucinations, insomnia, fever, and dehydration. To prevent withdrawal syndrome, patients are treated with a dose of phenobarbital equivalent to one-third of the daily dose of amobarbital on which they are dependent. This initial dose of phenobarbital is decreased by 30 milligrams per day until the patient's system is clear of drugs.

See also **Barbiturates.**

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AMOTIVATIONAL SYNDROME.

The term *amotivational syndrome* is often used interchangeably with *apathy syndrome*. Both terms refer to a set of characteristics that have been associated with the use of marijuana, cocaine, and inhalants.

Based on experiments conducted in the 1960s and 1970s, amotivational syndrome is characterized by a broad range of symptoms, including general apathy, lethargy, severe reduction in activities, difficulty in carrying out long-term plans, depression, and an inability to concentrate. The condition has long been associated with chronic marijuana use. Two studies conducted in the absence of controlled conditions linked amotivational syndrome to preexisting or coexisting mood disorders (i.e. anxiety, depression). In an early study (Kupfer et al., 1973), researchers suggested that amotivational syndrome might be a manifestation of pre-existing mood disorders, making individuals more susceptible to the syndrome. Specifically, they found that individuals who used marijuana frequently (i.e. three or more times a week) had discernible characteristics such as depression and lower energy levels. In a more recent study, R. E. Musty and L. Kaback (1995) investigated symptoms of depression among chronic heavy users (medians: daily use for six years) and light users (medians: several times per month for 4.5 years). They concluded that amotivational symptoms observed among chronic heavy marijuana users in this clinical sample were primarily caused by coexisting depression. Experiments conducted under controlled laboratory conditions, meanwhile, have offered mixed results regarding the amotivational effects of marijuana (Foltin et al., 1990; Kagel et al., 1980). A 2002 study by D. R. Cherek and colleagues aroused the suspicion that one factor that may contribute to the mixed results of other studies is the lack of operationally defined motivation. By defining motivation in precise behavioral terms, Cherek and colleagues found acute amotivational symptoms following marijuana smoking among occasional users (one to four times per month).

Apathy refers to a set of symptoms that includes anhedonia (an inability to experience pleasure from normally pleasurable events), reduced initiative, and decreased spontaneous activity. In the neurological literature, apathy is generally considered the result of decreased function in the subcortical regions, particularly a reduction in dopamine, a brain chemical associated with pleasure and motivation. Apathy is also exhibited in individuals diagnosed with frontal-subcortical disorders such as Parkinson's disease and HIV dementia. In a 2006 study examining prefrontal cortex function, Antonio Verdejo-García and colleagues found that substance-dependent individuals exhibited greater behavioral problems across different areas—including apathy, disinhibition, and executive dysfunction—than healthy individuals. In addition, Ari Kalechstein and colleagues (2002) suggested that, independent of depression, apathy was exhibited during the initial phases of abstinence for some cocaine-dependent individuals. In a 2005 study, Thomas Newton and colleagues found that following acute administration of a high dose of cocaine, apathy predicted hedonic (self-reported "High") but not craving response to cocaine. Patients with high apathy reported increased hedonic response. Similar to Kalechstein and colleagues' findings (2002), the reported effects were not due to depression.

Neither the amotivational syndrome nor the apathy syndrome is included in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (1994), and future research is needed to illuminate the role these conditions play in drug addiction and recovery. These findings have the potential to warrant dopamine-enhancing treatment for substance-dependent individuals.

See also **Cocaine; Depression; Dopamine; Marijuana (Cannabis).**

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AMPHETAMINE. Amphetamine was first synthesized in 1887, but its central nervous system (CNS) stimulant effects were not noted at that time. After rediscovery, in the early 1930s, its use as a respiratory stimulant was established and its properties as a central nervous system stimulant were described. Reports of abuse soon followed. As had occurred with cocaine products when they were first introduced in the 1880s, amphetamine was promoted as being an effective cure for a wide range of ills without any risk of addiction. The medical profession enthusiastically explored the potentials of amphetamine, recommending it as a cure for everything from alcohol hangover and depression to the vomiting of pregnancy and weight reduction. These claims that it was a miracle drug contributed to public interest in the amphetamines, and they rapidly became the stimulant of choice—since they were inexpensive, readily available, and had a long duration of action.

Derivatives of amphetamine, such as methamphetamine, were soon developed and both oral and intravenous preparations became available for therapeutic uses. Despite early reports of an occasional adverse reaction, enormous quantities were consumed in the 1940s and 1950s, and their liability for abuse was not recognized. During World War II, the amphetamines, including methamphetamine, were widely used as stimulants by the military in the United States, Great Britain, Germany, and Japan, to counteract fatigue, to increase alertness during battle and night watches, to increase endurance, and to elevate mood. It has been estimated that approximately 200 million Benzedrine (amphetamine) tablets were dispensed to the U.S. armed forces during World War II. In fact, much of the research on performance effects of the amphetamines was carried out on enlisted personnel during this period, as the various countries sought ways of maintaining an alert and productive armed force. Although amphetamine was found to increase alertness, little data were collected supporting its ability to enhance performance.

Since 1945, use of the amphetamines and cocaine appears to have alternated in popularity, with several stimulant epidemics occurring in the United States. There was a major epidemic of amphetamine and methamphetamine abuse (both oral and intravenous) in Japan right after the war. The epidemic was reported to have involved, at its peak, some half-million users and was related to the release with minimal regulatory controls of huge quantities of surplus amphetamines that had been made for use by the Japanese military. Despite this experience, there were special regulations governing their manufacture, sale, or prescription in the United States until 1964 (Hall et al., 1991).

The first major amphetamine epidemic in the United States peaked in the mid-1960s, with approximately 13.5 percent of the university population estimated, in 1969, to have used amphetamines at least once. By 1978, use of the amphetamines had declined substantially, contrasting with the increase of cocaine use by that time. The major amphetamine of concern in the United States in

Homemade amphetamine sulfate. DAVID HOFFMAN PHOTO LIBRARY/ALAMY.

the 1990s is methamphetamine, with pockets of "ice" (smoked methamphetamine) abuse.

Amphetamines are now controlled under Schedule II of the Controlled Substances Act. Substances classified within this schedule are found to have a high potential for abuse as well as currently accepted medical use within the United States. Amphetamine, methamphetamine, cocaine, methylphenidate, and phenmetrazine are all stimulants included in this schedule.

MEDICAL UTILITY

Amphetamines are frequently prescribed for the treatment of narcolepsy, obesity, and for childhood attention deficit disorder. They are clearly efficacious in the treatment of narcolepsy, one of the first conditions to be successfully treated with these drugs. Although patients with this disorder can require large doses of amphetamine for prolonged periods of time, attacks of sleep can generally be prevented. Interestingly, tolerance does not seem to develop to the therapeutic effects of these drugs, and most patients can be maintained on the same dose for years.

Although the amphetamines have been used extensively in the treatment of obesity, considerable evidence exists for a rapid development of tolerance to the anorectic (appetite loss) effects of this drug, with continued use having little therapeutic effect. These drugs are extremely effective appetite suppressants, but after several weeks of use the dose must be increased to achieve the same appetite-suppressant effect. People remaining on the amphetamines for prolonged periods of time to decrease food intake can reach substantial doses, resulting in toxic side effects (e.g., insomnia, irritability, increased heart rate and blood pressure, and tremulousness). Therefore, these drugs should only be taken for relatively short periods of time (4–6 weeks). In addition, long-term follow-up studies of patients who were prescribed amphetamines for weight loss have not found any advantage in using

this medication to maintain weight loss. Data indicate that weight lost under amphetamine maintenance is rapidly gained when amphetamine use is discontinued. In addition to the lack of long-term efficacy, the dependence-producing effects of amphetamines make them a poor choice of maintenance medication for this problem.

The use of amphetamines in the treatment of attention deficit disorders in children, remains extremely controversial. It has been found that the amphetamines have a dramatic effect in reducing restlessness and distractibility as well as lengthening attention span, but there are side effects. These include reports of growth impairment in children, insomnia, and increases in heart rate. Those promoting their use point to their potential benefits and they advocate care in limiting treatment dose and duration. Opponents of their use, while agreeing that they provide some short-term benefits, conclude that these do not outweigh their disadvantages. Amphetamine therapy has also been attempted, but with little success, in the treatment of Parkinson's disease, and both amphetamine and cocaine have been suggested for the treatment of depression, although the evidence to support their efficacy does not meet current standards demanded by the U.S. Food and Drug Administration.

PHARMACOLOGY

The amphetamines act by increasing concentrations of the neurotransmitters dopamine and norepinephrine at the neuronal synapse, thereby augmenting release and blocking uptake. It is the augmentation of release that differentiates amphetamines from cocaine, which also blocks uptake of these transmitters. Humans given a single moderate dose of amphetamine generally show an increase in activity and talkativeness, and they report euphoria, a general sense of well-being, and a decrease in both food intake and fatigue. At higher doses repetitive motor activity (i.e., stereotyped behavior) is often seen, and further increases in dose can lead to convulsions, coma, and death. This class of drugs increases heart rate, respiration, diastolic and systolic blood pressure, and high doses can cause cardiac arrhythmias. In addition, the amphetamines have a suppressant effect on both rapid eye movement sleep (REM)—the stage of sleep associated with dreaming—and total sleep. The half-life of amphetamine is about ten hours, quite long when compared to a stimulant like cocaine, which has a half-life of approximately one hour, or even methamphetamine which has a half-life of about five hours.

The amphetamine molecule has two isomers: the *d*-(+) and *l*-(−) isomers. There is marked stereo-selectivity in their biological actions, with the *d*-isomer (dextroamphetamine) considerably more potent. For example, it is more potent as a locomotor stimulant, in inducing stereotyped behavior patterns, and in eliciting central nervous system excitatory effects. The isomers appear to be equipotent as cardiovascular stimulants. The basic amphetamine molecule has been modified in a number of ways to accentuate various of its actions. For example, in an effort to obtain appetite suppressants with reduced cardiovascular and central nervous system effects, structural modifications yielded such medications as diethylproprion and fenfluramine, while other structural modifications have enhanced the central nervous system stimulant effects and reduced the cardiovascular and anorectic actions, yielding medications such as methylphenidate and phenmetrazine. These substances share, to a greater or lesser degree, the properties of amphetamine.

TOXICITY

A major toxic effect of amphetamine in humans is the development of a schizophrenia-like psychosis after repeated long-term use. The first report of an amphetamine psychosis occurred in 1938, but the condition was considered rare. Administration of amphetamine to normal volunteers with no histories of psychosis (Griffith et al., 1970) resulted in a clear-cut paranoid psychosis in five of the six subjects who received *d*-amphetamine for one to five days (120–220 mg/day), which cleared when the drug was discontinued. Unless the user continues to take the drug, the psychosis usually clears within a week, although the possibility exists for prolonged symptomology. This amphetamine psychosis has been thought to represent a reasonably accurate model of schizophrenia, including symptoms of persecution, hyperactivity and excitation, visual and auditory hallucinations, and changes in body image. In addition, it has been suggested that there is sensitization to the development of a stimulant psychosis—once an individual has experienced this toxic effect, it is readily reinitiated, sometimes at lower doses and even following long drug-free periods.

Amphetamine abusers taking repeated doses of the drug can develop repetitive behavior patterns which persist for hours at a time. These can take the form of cleaning, the repeated dismantling of small appliances, or the endless picking at wounds on the extremities. Such repetitive stereotyped patterns of behavior are also seen in nonhumans administered repeated doses of amphetamines and other stimulant drugs, and they appear to be related to dopaminergic facilitation. Cessation of amphetamine use after high-dose chronic intake is generally accompanied by lethargy, depression, and abnormal sleep patterns. This pattern of behavior, opposite to the direct effects of amphetamine, does not appear to be a classical abstinence syndrome. The symptoms may be related to the long-term lack of sleep and food intake that accompany chronic stimulant use as well as to the catecholamine depletion that occurs as a result of chronic use.

Animals given unlimited access to amphetamine will self-administer it reliably, alternating days of high intake with days of low intake. They become restless, tremulous, and ataxic, eating and sleeping little. If allowed to continue self-administering the drug, most will take it until they die. Animals maintained on high doses of amphetamines develop tolerance to many of the physically and behaviorally debilitating effects, but they also develop irreversible damage in some parts of the brain, including long-lasting depletion of dopamine. It has been suggested that the prolonged anhedonia seen after long-term human amphetamine use may be related to this, although the evidence for this is not very strong.

BEHAVIORAL EFFECTS

Nonhumans. As with all psychomotor stimulant drugs, at low doses animals are active and alert, showing increases in responding maintained by other reinforcers, but often decreasing food intake. Higher doses produce species-specific repetitive behavior patterns (stereotyped behavior), and further increases in dose are followed, as in humans, by convulsions, hyperthermia, and death. Tolerance (loss of response to a certain dose) develops to many of amphetamine's central effects, and cross-tolerance among the stimulants has been demonstrated in rats. Thus, for example, animals tolerant to the anorectic effects of amphetamine also show tolerance to cocaine's anorectic effects. Although there is tolerance development to many of amphetamine's effects, sensitization develops to amphetamine's effects on locomotor activity. Thus, with repeated administration, doses of amphetamine that initially did not result in hyperactivity or stereotypy can, with repeated use, begin to induce those behaviors when injected daily for several weeks. In addition, there is cross-sensitization to this effect, such that administration of one stimulant can induce sensitization to another one. In contrast to cocaine, however (in which an increased sensitivity to its convulsant effects develops with repeated use), amphetamines have an anticonvulsive effect.

Learned behaviors, typically generated by operant schedules of reinforcement, are generally affected by the amphetamines in a rate-dependent fashion. Thus, behaviors that occur at relatively low rates in the absence of the drug tend to be increased at low-to-moderate doses of amphetamine, while behaviors occurring at relatively high frequencies tend to be suppressed by those doses of amphetamine. In addition, with high doses most behaviors tend to be suppressed. As is seen with other stimulants, such as cocaine, environmental variables and behavioral context can play a role in modulating these effects. For example, behavior under strong stimulus control shows tolerance to repeated amphetamine administration much more rapidly than does behavior under weak stimulus control. In addition, if the amphetamine-induced behavioral disruption has the effect of interfering with reinforcement delivery, tolerance to that effect develops rapidly. Tolerance does not develop to the amphetamine-induced disruptions when reinforcement density is increased or remains the same.

Amphetamines can serve as reinforcers in nonhumans and, as described above, can produce severely toxic consequences when available in an unlimited fashion. However, when available for a few hours a day, animals will take them in a regular fashion, showing little or no tolerance to their reinforcing effects.

Humans. A substantial number of studies have been carried out evaluating the effects of amphetamines on learning, cognition, and other aspects of performance. The data indicate that under most conditions the amphetamines are not general performance enhancers. When there is improvement in

performance associated with amphetamine administration, it can usually be attributed to a reduction in the deterioration of performance due to fatigue or boredom. Attention lapses that impair performance after sleep deprivation appear to be reduced by amphetamine administration; however, as sleep deprivation is prolonged, this effect is reduced. A careful review of the literature in this area (Laties & Weiss, 1981) concluded that improvement is more obvious with complex, as compared with simple, tasks.

In addition, in trained athletes, whose behavior shows little variability, only very small improvements can be seen. Laties and Weiss have argued persuasively, however, that the small changes in performance induced by amphetamines can result in the 1 to 2 percent improvement that may make the difference in a close athletic competition. Although the facilitation in performance after amphetamine does not appear to be substantial, it is sufficient to "spell the difference between a gold medal" and any other. Unfortunately, such data have led athletes to take stimulants prior to athletic events, particularly those in which strenuous activity is required over prolonged periods (e.g., bicycle racing), leading to hyperthermia, collapse, and even death in some cases.

The mood-elevating effects of the amphetamines are generally believed to be related to their abuse. Their use is accompanied by reports of increased self-confidence, elation, frequently euphoria, friendliness, and positive mood. When amphetamine is administered repeatedly, tolerance develops rapidly to many of its subjective effects (such that the same dose no longer exerts much of an effect). This means that the user must take increasingly larger amounts of amphetamine to achieve the same effect. As with nonhuman research subjects, there is however, little or no evidence for the development of tolerance to amphetamine's reinforcing effects.

Experienced stimulant users, given a variety of stimulant drugs, often cannot differentiate among cocaine, amphetamine, methamphetamine, and methlyphenidate—all of which appear to have similar profiles of action. Since these drugs have different durations of action, however, it becomes easier to make this differentiation over time.

ABUSE

In the United States in the 1950s, nonmedical amphetamine use was prevalent among college students, athletes, truck drivers, and housewives. The drug was widely publicized by the media when very little evidence of amphetamine toxicity was available. Pills were the first form to be widely abused. Use of the drug expanded as production of amphetamine and methamphetamine increased significantly, and abusers began to inject it. An extensive black market in amphetamines developed, and it has been estimated that 50 to 90 percent of the quantity commercially produced was diverted into illicit channels. In the 1970s, manufacture of amphetamines was substantially curtailed, amphetamines were placed in Schedule II of the Controlled Substances Act, and abuse of these substances was substantially reduced. Perhaps only by coincidence, as amphetamine use declined, cocaine use increased.

The amphetamines, as with other stimulants, are generally abused in multiple-dose cycles (i.e., binges), in which people take the drug repeatedly for some period of time, followed by a period in which they take no drug. Amphetamines are often taken every three or four hours for periods as long as three or four days, and dosage can escalate dramatically as tolerance develops. Like cocaine binges, these amphetamine-taking occasions are followed by a "crash" period in which the user sleeps, eats, and does not use the drug. Abrupt cessation from amphetamine use is usually accompanied by depression. Mood generally returns to normal within a week, although craving for the drug can last for months.

There is little evidence for the development of physical dependence to the amphetamines. Although some experts view the "crash" (with lethargy, depression, exhaustion, and increased appetite) that can follow a few days of moderate-to-high dose use as meeting the criteria for a withdrawal syndrome, others believe that the symptoms can also be related to the effects of chronic stimulant use. When using stimulants people do not eat or sleep very much and, as well, catecholamine depletion may well be contributing to these behavioral changes.

TREATMENT

As of the mid-1990s, little information is available about the treatment of amphetamine abusers, and no reports of successful pharmacological interventions exist in the treatment literature. As with cocaine abuse, the most promising non-pharmacological approaches

include behavioral therapy, relapse prevention, rehabilitation (e.g., vocational, educational, and social-skills training), and supportive psychotherapy. Unlike cocaine, however, minimal clinical trials with potential treatment medications for amphetamine abuse have been carried out. The few that have been attempted report no success in reducing a return to amphetamine use.

See also **Amphetamine Epidemics, International; Pharmacokinetics: General; Treatment: An Overview.**

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MARIAN W. FISCHMAN

AMPHETAMINE EPIDEMICS, INTERNATIONAL.

The history and epidemiology of amphetamines illustrate particularly well the way in which the medical use and nonmedical use (or "abuse") of drugs can be intimately linked, both in terms of supply and other factors that drive demand. Amphetamines were introduced as medicines in the late 1930s and 1940s, leading to an epidemic of pharmaceutical overuse, frank abuse, and addiction by the 1950s in much of the developed world. In certain nations the drugs were controlled quite early, but medical recognition of the widespread excessive consumption and deleterious effects of amphetamines was, in general, belated. Their licit use was only curtailed internationally after 1970, promoting a global shift to nonmedical use of illicitly manufactured amphetamines and, where available, cocaine. Amphetamine use has since remained endemic throughout much of the world.

The years since approximately 1990 have seen an expansion in the illicit supply of methamphetamine in particular, and surges in the nonmedical use of (and addiction to) amphetamine-type stimulants in several nations and regions. Not all of these surges can be described as "epidemics," if the term is used to denote a conversion of nonusers to users, in a strict analogy to infectious disease. However, switching to amphetamines from other drugs, or the intensification of use among less frequent users of amphetamines, both have important public health consequences, so it might be counterproductive to observe the analogy too strictly.

This period of increase in nonmedical amphetamine usage has also seen a parallel resurgence in the medical consumption and supply of amphetamines and related stimulants in some nations, especially for attention deficit/hyperactivity disorder (ADHD). The use of hallucinogenic amphetamines of the "Ecstasy" variety has similarly tracked the recent rises in medical and nonmedical amphetamine use. These drugs are treated elsewhere in this encyclopedia.

THE INTRODUCTION OF AMPHETAMINES IN THE 1930S AND 1940S

Pharmacologically, the amphetamines are best regarded as synthetic analogs of adrenaline and ephedrine, both of which provided the impetus for their discovery. Like adrenaline (and noradrenaline), they promote wakefulness and stimulate certain functions in the central nervous system, as well as peripheral functions mediated by sympathetic nerves—hence their characterization as "sympathomimetics." Credit for the first discovery of the amphetamines as drugs belongs to the Japanese pharmacologist Nagai Nagayoshi (1844–1929), who in the 1890s produced methamphetamine in his research on ephedrine, which he had previously identified as the active ingredient in the medicinal herb ephedra. Though ephedrine was taken up in

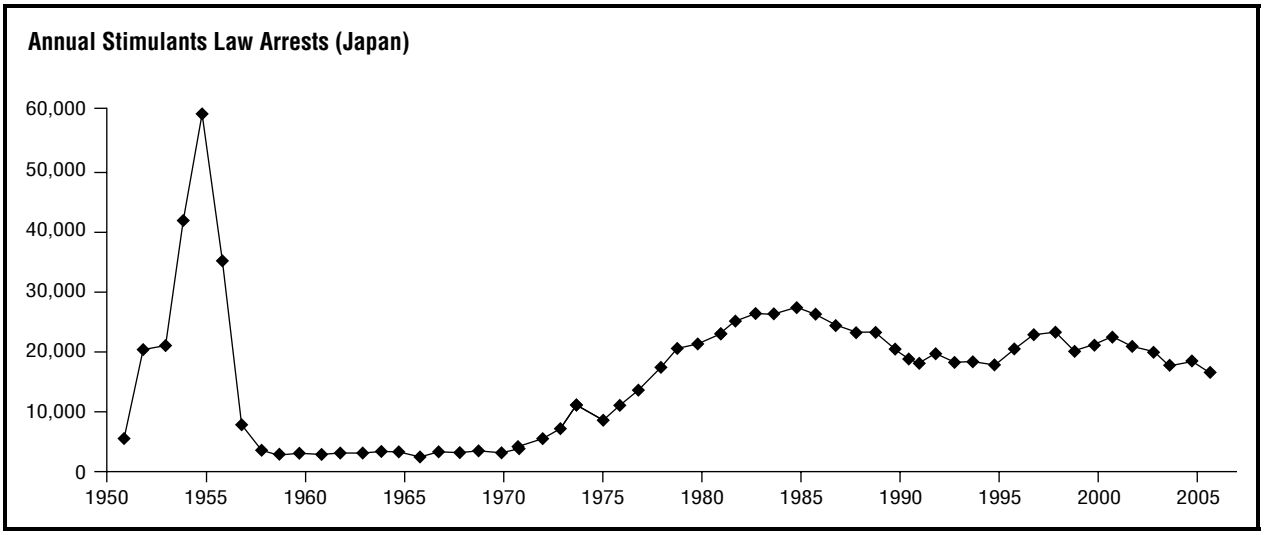

Figure 1. Annual stimulant law violations, Japan. The initial outbreak of methamphetamine injection, and gradual expansion of endemic nonmedical usage patterns, as traced by arrests after 1949, when pharmaceutical methamphetamine was made a controlled substance in Japan. (Adapted from Brill and Hirose, 1969; United Nations, 2007.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Japanese medicine, methamphetamine was not, and this work appears to have gone unnoticed in the West. In the 1920s, ephedrine was independently "discovered" and introduced into Western medicine, where it quickly became popular as a decongestant and an asthma remedy, for which it was more convenient than adrenaline because of its oral availability.

In 1929 the independent California biochemist Gordon Alles synthesized amphetamine in a pursuit of a better oral anti-asthmatic, and his animal experiments and self-experimentation revealed both its sympathomimetic and central stimulant actions, including euphoria. In 1932 Alles received a patent on the orally available salts of amphetamine for use as medicines. Shortly thereafter, the Smith, Kline and French (SKF) drug firm acquired Alles's patent, having taken their own patent on the medical use of the oily base form of amphetamine in 1933.

By 1934, SKF had introduced the Benzedrine Inhaler, a tube containing over 300 milligrams of oily amphetamine base, as an inexpensive over-the-counter congestion remedy throughout North America. Not long afterwards they introduced the inhaler in Latin America and Europe. From 1935 SFK sponsored clinical research to explore various possible uses for their Benzedrine Sulfate oral amphetamine product, including multiple sclerosis; dysmenhorrea, or painful menstruation; and bed-wetting. By late 1937 the firm had settled on, and received American Medical Association (AMA) approval for, three initial indications: narcolepsy, post-encephalytic Parkinsonism, and minor depression. For the next decade these indications, and especially depression, would represent the drug's main official uses and the focus of SKF's marketing. At the onset of the Second World War, amphetamine's use as an antidepressant was becoming established in North America and much of Europe, while in Germany at least two drug firms had begun marketing methamphetamine, an old drug lacking patent protection, along the same lines.

During the Second World War, amphetamines were distributed by the military on all sides to maintain wakefulness and for the purported improvement of performance under fatigue. In the Blitzkrieg of late 1939 and early 1940, the German military consumed something on the order of 10 million tablets of methamphetamine monthly. By late 1940, German military consumption dropped an order of magnitude, after perfunctory early studies that showed improved scores on certain tests of mental and hand-eye performance were not borne out by more careful research. In addition, experience with the drug in combat pointed to problems with impaired judgment, post-drug exhaustion, and abuse. Usage dropped still further in 1941, when Germany placed both

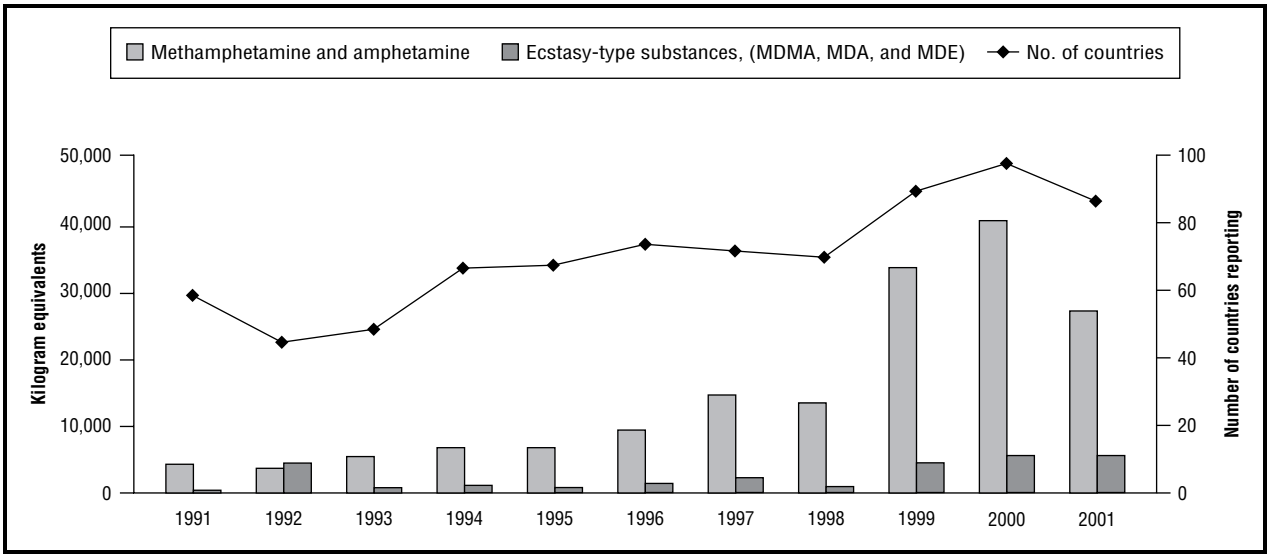

Figure 2. Reported global seizures of amphetamine-type stimulants, 1999–2001. Global drug seizure data indicate increased illicit supplies of amphetamines, largely from East Asia. (Source: United Nations, 2003.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

methamphetamine and amphetamine under narcotics regulation, and again in 1942, with the official recognition that these amphetamines were dangerously addictive. The Japanese military appears to have used oral methamphetamine throughout the war, while both the British and American militaries used amphetamine, even though they were aware of the German change of policy. However, in contrast to American military consumption, British military usage seems to have become more cautious later in the war, following experiences similar to Germany's: Amphetamine's apparent performance-enhancing effects were not consistently demonstrable in careful lab experimentation, and mainly reflected optimism and distorted self-perception due to the drug's subjective effects.

In Japan, the immediate postwar years saw an epidemic of nonmedical methamphetamine use, promoted by the familiarity of the population with the drug from military usage, by austerity and social dislocation caused by the war, and by the easy availability of the drug. In 1946 the injection abuse of the drug was already becoming common, and in 1949 the government sharply reduced pharmaceutical supplies and made illicit amphetamine possession and sale illegal under special stimulant control legislation. In 1954 the Japanese methamphetamine epidemic reached its peak at an estimated 2 million abusers in a population not much higher than 80 million. Usage declined sharply thereafter, but this was followed by a serious increase in heroin use, largely driven by the easy switch from amphetamine injection.

Widespread wartime use of amphetamine may have similarly begun a postwar epidemic of nonmedical amphetamine use in the United States, albeit one less visible because it lacked the stigma associated with injection. A landmark 1945 study of military personnel imprisoned for mainly minor infractions found not only that oral consumption of high doses of amphetamine base from Benzedrine Inhalers was widespread and that many had begun abusing the inhalers in military service before imprisonment, but that military exposure to Benzedrine (mainly in tablet form provided by a medical officer) was more than five times more common among abusers than non-abusers. Thus, official military use of amphetamine appears to have significantly increased the incidence of amphetamine abuse among American servicemen. Such abuse also grew among young American civilians in the 1940s, as documented by Beatnik writers and jazz musicians. Although the high abuse potential of amphetamine inhalers was known to North American law enforcement by the end of the Second World War, the products were not entirely removed from over-the-counter sale until the early 1960s.

THE POSTWAR PANDEMIC OF AMPHETAMINE USE

The medical use of amphetamine also began to grow dramatically in the war years. Its magnitude in the United States at the end of the war is revealed by a patent lawsuit between SKF and a smaller firm named Clark & Clark, which had been producing both imitation Benzedrine Sulfate and colorful pills for use, still unapproved, in weight loss. In late 1945 the two firms together were selling approximately 30 million tablets a month for civilian use in the United States, of which perhaps half was for depression and related psychiatric indications. Assuming that all these tablets were taken on the typical two tablets per day schedule, there were at least half a million Americans using oral amphetamines medically in 1945. These are conservative figures that disregard the production by other firms of amphetamine and (unpatented) methamphetamine, as well as the fact that amphetamine was probably consumed, on average, less frequently than twice daily. After winning the legal dispute and keeping its patent monopoly on amphetamine, and then achieving approval to market the drug for weight loss in 1947, SKF's sales of Benzedrine tablets and Dexedrine brand dextroamphetamine tablets more than tripled between 1945 and 1949. Medical amphetamine use similarly flourished in other developed countries during the immediate postwar period, and the drug became widely accepted as an everyday "antidepressant" (a term that first appears in late 1940s Benzedrine advertising).

The United States was the postwar world's leading producer and consumer of amphetamines. According to voluntary production surveys by the U.S. Food and Drug Administration (FDA), annual production of oral amphetamines by U.S. firms increased nearly fourfold between 1949, when SKF's key patent expired and competitors entered the market, and 1953. In 1962 the FDA's estimate of national production (and consumption) had reached about 8 billion 10-milligram tablets of amphetamine and methamphetamine salts. This translates into more than 40 tablets per American per year, and FDA estimates would grow only slightly by the end of the 1960s. Thus, by the beginning of the 1960s, the American market was essentially saturated with amphetamines, leading to significant iatrogenic addiction problems—although it would take another decade for significant alarm at this situation to emerge. In the early 1960s the large-scale diversion of pharmaceutical amphetamines to black-market channels for nonmedical use was also well-established.

The best evidence regarding the European countries in which medical amphetamine use flourished during the postwar period comes from the United Kingdom. A study of retail prescriptions filled in the Newcastle area during 1960 found that about 3 percent were for oral amphetamines, consistent both with U.K. national prescribing figures at the time and with contemporary prescribing in the United States. The most popular preparation was SKF's Dexamyl (or Drinamyl), a blend of dextroamphetamine and the barbiturate amobarbital. One third of amphetamine prescriptions were for weight loss, a third for clear-cut psychiatric disorders (e.g., depression, anxiety), and the remaining third for ambiguous, mostly psychiatric and psychosomatic complaints. The typical amphetamine patient was between 36 and 45 years old and female. Indeed, based on the Newcastle data, it seems that in 1960, females were twice as likely as males to receive amphetamine for psychiatric adjustment per doctor visit. Furthermore, between 2 percent and 3 percent of the total population of Newcastle must have received amphetamine prescriptions in the course of a year and, shockingly, 6.7 percent to 10 percent of these were judged by their doctors to be dependent to some degree.

With such large quantities of amphetamines being consumed medically and nonmedically in the 1950s and 1960s, the negative effects of the drugs naturally became more apparent. Amphetamine psychosis was first observed in the 1930s among long-term narcoleptic users of the drug, and individual case reports mounted during the 1940s and early 1950s, both among those prescribed tablets and those abusing inhalers. Initially, psychotic episodes were attributed to latent schizophrenia "unmasked" by the drug, or to another psychiatric defect in the victim. The definitive 1958 study of the condition by psychiatrist Philip Connell made this view untenable. A typical set of paranoid symptoms (e.g., sinister voices emanating from toilet bowls, cars or helicopters following one's every move) were uniform across a wide variety of personality types, arguing against any shared predisposing feature of mentality or neurology. In addition, the psychosis generally took time to

develop, suggesting a cumulative effect. Although almost all of the 40 patients described by the British psychiatrist had engaged in some high-dose nonmedical use before their crises, a large proportion had first taken amphetamines by prescription. They could not, therefore, be stigmatized as deviant thrill-seekers. Finally, patients recovered fully a week or two after they ceased amphetamine use, proving they were never schizophrenics. Amphetamine psychosis clearly could happen to any individual, and eventually it would, given enough use of the drug.

Nevertheless, amphetamines for both weight loss and everyday psychological distress retained many medical defenders, who tended to argue that even if amphetamines caused psychosis when excessively consumed, character defects were responsible for the excessive consumption of amphetamines. Thus these drugs could still safely be prescribed to most people. This reasoning overlooked the fact that amphetamines are addictive, and indeed they were not recognized as such by pharmacologists when the drugs were initially introduced. However, new definitions of drug dependency promulgated by the World Health Organization and other expert bodies since the late 1950s moved the concept away from an older opiate-based model, in which physical withdrawal was definitive, to one centered on compulsive drug use and an erosion of psychosocial function. As this new concept of drug dependency took hold in the 1960s, it became clearer that amphetamine-type stimulants were seriously dependency-producing, and that they could therefore no longer be defended as "merely habituating," like caffeine.

REACTIONS TO THE FIRST EPIDEMIC IN THE 1960S

The realization that amphetamine pharmaceuticals presented a major abuse and dependency hazard came earlier to some countries. As noted, Nazi Germany had declared both amphetamine and methamphetamine to be addictive narcotics early in the Second World War, and in 1944, neutral Sweden followed suit when significant oral abuse first emerged. Swedish medical use of these amphetamines remained low thereafter, though pharmaceutical smuggling from neighboring countries maintained supply on the black market. However, when supposedly safer new amphetamines were introduced in the later 1950s—phenmetrazine (trade name Preludin, for dieting) and methylphenidate (Ritalin, for depression)—they were widely prescribed, and their injection abuse soon exploded. These pharmaceuticals were taken off the medical market in 1965 and 1968, respectively. Still, in 1970 the number of addicted stimulant injectors in Stockholm was estimated at about 0.5 percent of the population (said to be comparable to heroin addiction prevalence in New York City at the time), and these abusers were primarily supplied with smuggled pharmaceutical amphetamine.

During the 1960s the overlapping problems of nonmedical amphetamine use, overmedication, and iatrogenic addiction began raising alarms in the United Kingdom and, eventually, the United States. Apart from the medical addiction explored by the Newcastle studies, purely recreational oral abuse of pharmaceutical amphetamines became widespread in London's Soho district and other areas associated with youth subcultures in the middle of the decade (among whom Drinamyl was especially popular and known as "Purple Heart"). Legislation making it illegal to possess the pills without a prescription was enacted, without any dramatic impact. Family practitioners organized their own prescribing moratoria, and these voluntary measures began to reduce amphetamine supplies in the United Kingdom to some extent by the end of the decade.

In the United States, amphetamines figured prominently in a series of scandals and Congressional hearings throughout the 1960s in connection with topics such as the role of truckers in trafficking diverted pharmaceuticals, the overmedication of women for weight loss, and polydrug abuse and addiction in Vietnam (where servicemen were supplied by the military with large quantities of dextroamphetamine). Nonmedical drug use generally became an increasingly important public issue, as the social changes of the 1960s moved the phenomenon from the social margins to the spotlight. Thus, an amphetamine injection outbreak in the San Francisco "hippie" enclave of Haight-Ashbury in 1967 and 1968 garnered enormous national press and political attention. "Speed freaks," as the amphetamine injectors were known within the hippie counterculture, engaged in a distinctive pattern of collective and frequent injection to multiply the initial "rush" experience, which they continued

until total exhaustion and collapse ensued. American "speed freaks" of the late 1960s seemed to prefer methamphetamine, and much of this was supplied from small-scale illicit labs, although the great majority of amphetamines sold on the street at the time were oral pharmaceutical preparations. Thus, pharmaceutical oversupply remained the greatest source of nonmedical amphetamine problems through the end of the 1960s.

While defenders of pharmaceutical industry interests attempted to keep the issues separate, the frightening but relatively rare problem of injection abuse and the much larger problem of prescription drug overuse were associated politically as well as epidemiologically. At the end of the 1960s, the same type of scandal that had arisen regarding the overmedication of women with minor tranquilizers emerged around amphetamines, particularly as dispensed in diet pill form. One of the first modern drug use surveys measured strictly medical past-year amphetamine use in 1970 at 5 percent of American adults, while a more thorough survey of both medical and nonmedical amphetamine use in New York State found that 6.5 percent of the state's 13.8 million residents over 14 years of age had used amphetamines in the past 6 months, and of these, 39 percent had used them nonmedically. Virtually all the nonmedical users were taking pharmaceutical amphetamines, and legitimately prescribed amphetamines accounted for much of the nonmedical use. As in Newcastle, the typical user was middle-aged. Extrapolating to the United States as a whole, the New York prevalence figures would indicate that, in 1970, about 10 million Americans used amphetamines either medically or nonmedically (or both).

Accepting the medical dependency rates derived from the Newcastle studies, a conservative measure as applied to an American population containing many nonmedical users more freely supplied with amphetamines, the United States in 1970 must have contained around a million people suffering amphetamine dependency to some extent, as well as over 300,000 addicted or amphetamine-dependent individuals, strictly defined. The vast majority of these dependent individuals were supplied by the pharmaceutical industry, and many, perhaps most, obtained at least some of their amphetamines by prescription. However, unlike their counterparts in Britain and some other countries, the American medical profession resisted limits on the drugs even after such facts became known. The AMA did not officially caution that dependency could develop from prescribed amphetamines until 1978.

LEGISLATION AND CONVENTION ON PSYCHOTROPIC SUBSTANCES, 1971

At the beginning of the 1970s a United Nations drug control treaty was instituted, expanding longstanding international opiate controls to cannabis and synthetic drugs of abuse, including the amphetamines. The 1971 Convention on Psychotropic Substances established the modern system of controlled substance "schedules" and required signatory nations to institute internal legal controls on designated drugs. Due to pharmaceutical industry lobbying, the initial U.S. legislation along these lines, the 1970 Comprehensive Drug Abuse Prevention and Control Act, included only a handful of rarely prescribed injectable methamphetamine products in Schedule II, leaving some 6,000 oral amphetamine and methamphetamine products in the much less restricted Schedule III. However, in 1971, U.S. narcotics authorities employed powers gained under the act to move all oral amphetamines, including methylphenidate and phenmetrazine, to Schedule II, where their prescriptions would be nonrefillable and subject to strict record keeping. Their production would also be limited to a quota adequate for medical demand. Prescription rates briefly soared when the changes were announced, but they fell to less than half their original levels when the changes came into effect.

Given the drop in prescriptions, narcotics authorities set 1972 U.S. amphetamine production quotas at one-fifth those of 1971 (one tenth officially reported medical production for 1969, and around one twentieth actual 1969 production), the equivalent of 400 million 10-milligram doses of amphetamine and methamphetamine salts. This was accomplished with the cooperation of the U.S. Federal Drug Administration, which was reevaluating the amphetamines as antidepressants and obesity drugs and would soon declare them of limited value for their most popular indications, leaving only narcolepsy and the then-rare pediatric condition now known as attention deficit hyperactivity disorder (ADHD).

Nonmedical amphetamine use was quickly overshadowed by rising cocaine use. Although nonmedical

amphetamine use remained endemic in the United States and elsewhere after 1971, it can still be said that the first global amphetamine epidemic was brought under some control through aggressive restrictions on pharmaceutical supplies of the drugs (along with law enforcement measures against illicit distributors), much like the Japanese methamphetamine outbreak of the early 1950s.

AMPHETAMINE'S RESURGENCE

While there has been much public discussion and alarm over a methamphetamine (or "meth") epidemic in the United States, Japan, Australia, and elsewhere since the 1990s, solid quantitative evidence does not unequivocally support a dramatic general upswing in the nonmedical use of amphetamines. Instead, it may be better to picture a fairly constant endemic "background" of amphetamine and methamphetamine use, punctuated locally by outbreaks or transitory intensifications of usage and increased addiction rates triggered by increased supply or social changes. To be sure, since the late 1990s there has been a general increase in global supplies, particularly of methamphetamine produced in China and Myanmar (Burma), which recently dislodged Holland from its longstanding position as the world's leading source of illicit amphetamines. This increase in supply has been associated with localized surges in amphetamine abuse and its public health impacts. For instance, high-purity crystalline methamphetamine (sometimes known as "ice") from such Asian sources was responsible for a sudden and destructive upsurge in methamphetamine use in Hawaii during the late 1980s.

In the mainland United States, increased supply—signaled by a rise in seizures of methamphetamine—has correlated with a distinct rise in emergency room mentions of amphetamines, especially since 2000. Usage was relatively higher in smaller cities and rural areas than in large cities, marking the importance of small-scale local manufacture along with Asian imports. A similar pattern holds for Australia, another nation with a longstanding amphetamine abuse tradition (and the second highest prevalence of nonmedical use in the world in the early 2000s; see Figure 3). In Thailand, which was leading the world in prevalence of nonmedical amphetamine use in the mid-2000s, the severe abuse and addiction problems are clearly tied to increases in large-scale illicit methamphetamine manufacture in the region.

On the other hand, in Japan, where amphetamines have long been the leading illicit drug of abuse, a dramatic increase in amphetamine-class drug seizures from 1999 to 2001—associated with the increase in large-scale East Asian methamphetamine manufacture—saw no increase in amphetamine abuse or related arrests in the general population. Thus, an increase in methamphetamine supply is not the only determinant of nonmedical amphetamine-use trends. It may be that Japan's longstanding familiarity with methamphetamine

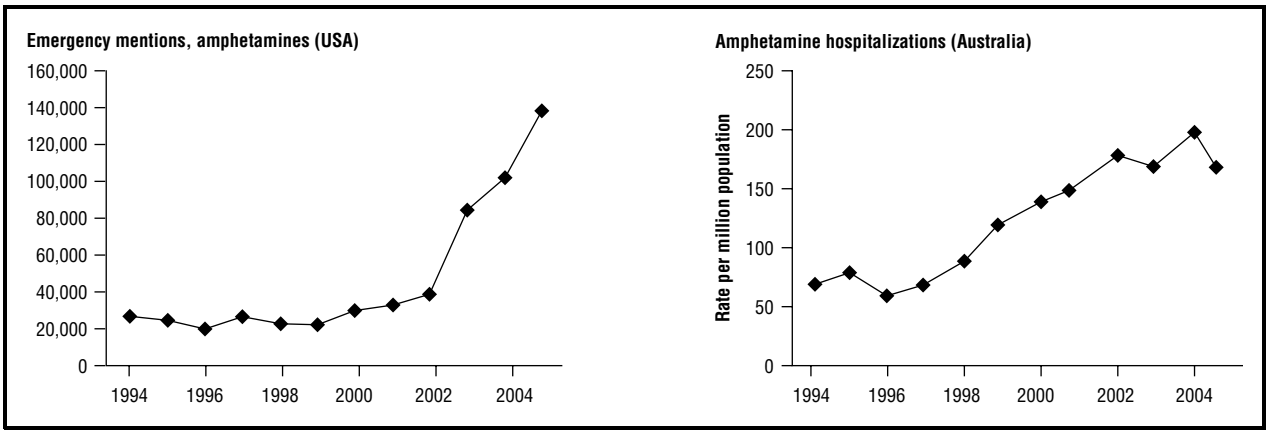

Figure 3. Trends in amphetamines-related hospitalization 1994–2005: (a) United States emergency room mentions of amphetamine-type stimulants (2003–2005 figures not directly comparable to pre–2003); (b) Australia amphetamine–related hospital separations. (Sources: Drug Abuse Warning Network and Roxburgh & Degenhardt.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

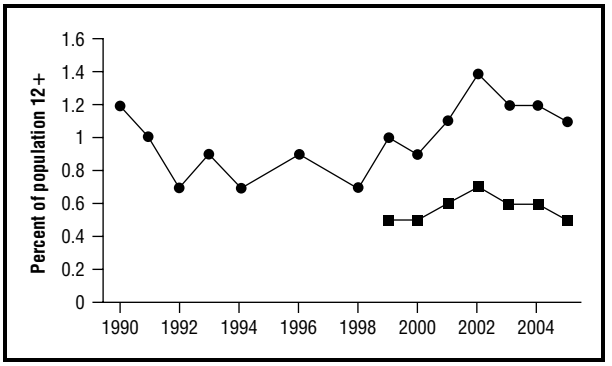

Figure 4. Nonmedical use of meth/amphetamines (USA). Past-year nonmedical use of amphetamine-type stimulants of all kinds (top) and of methamphetamine (bottom), 1990–2005. (Source: Substance Abuse and Mental Health Services Administration, National Survey on Household Drug Use Data.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

means that there are no potential user groups unfamiliar with the drug that might take it up when supplies become easier or cheaper to obtain.

Moreover, in some nations, methamphetamine is not the only major amphetamine-type drug of abuse. While amphetamine-related emergency room mentions in the United States increased over 40 percent between 1994 and 2002, the proportion attributed specifically to methamphetamine showed a consistent decline, from over 60 percent to barely 40 percent of the total. Prevalence data from U.S. household drug use surveys tell a similar story: At least since 1999, methamphetamine has only accounted for about half of the past-year nonmedical use of amphetamine-type stimulants—which overall saw a gentle decline during the early 1990s—followed by a recent rise back to former levels (see Figure 4).

As in the original epidemic, pharmaceutical amphetamines account for a large part of American amphetamine abuse in the first decade of the 21st century. Detailed analysis of U.S. survey data shows that approximately half of the 3 million past-year nonmedical users of amphetamines in 2002 through 2004 used only non-methamphetamine drugs, particularly methylphenidate and amphetamine medications for attention deficit disorder. Further, one-quarter of them had only used ADHD stimulants in their entire lives. Past-year nonmedical users strictly of pharmaceuticals for ADHD also accounted for half of the amphetamine-abusing Americans meeting some criteria for dependency, and for almost a third of the 300,000 who were dependent according to *DSM-IV* criteria.

Thus, the rise in nonmedical stimulant use in the United States during the late 1990s and early 2000s may owe much to the parallel, dramatic increase in methylphenidate and amphetamine prescribing for attention deficit disorder in the nation. The medical consumption of these two drugs grew 20-fold and 35-fold, respectively, between 1990 and 2005, and they have increasingly been prescribed for adolescents and adults. The relationship between ADHD medication prescribing and amphetamine abuse may involve both supply and the cultural determinants of demand. Widespread prescribing releases large supplies of amphetamines into the population, and thus increases the chance of misuse by those with prescriptions, and of resale to those without other access to the drugs. Both of these trends are well documented, especially at universities and high schools. (A similar leakage of supply occurred in the 1960s, with widespread prescribing of amphetamine antidepressants and diet pills.)

In addition, there is evidence that some current nonmedical users of amphetamines consume the drugs for essentially the same effects as those who take the drugs by prescription; namely, for a short-term improvement of working concentration. If so, then the medicalization of distractability, under the banner of attention deficit disorder (or attention deficit hyperactivity disorder), creates a demand that promotes amphetamine abuse. Finally, the return to normalization of the amphetamines as ADHD medications, after two decades of successful control through medical usage restrictions, inevitably undermines control efforts dependent on instilling a sense of danger around the drugs.

Evidently, even if methamphetamine supplies were somehow cut off completely, the longstanding endemic pattern of mostly oral nonmedical use of other amphetamines would, in many countries, continue. For stimulant addiction and its sequelae (such as amphetamine psychosis) to be fully controlled, licit amphetamine-type pharmaceuticals would also have to be entirely eliminated from circulation, because these represent a significant source of supply and a cultural priming factor for amphetamine abuse. Nevertheless, the rise in the

world supply of methamphetamine raises special concerns because, in many populations of users, the dominant form of administration is intravenous, and because the use of the drug is still associated with frequent, and collective injection (as was the case among the "speed freaks" of the late 1960s); multiple sexual partners; and risky sexual practices. For example in Russia, which has serious local outbreaks of both amphetamine abuse and AIDS, amphetamine use is associated with higher rates of HIV infection than heroin use without amphetamines. Thus, syringe-exchange programs and similar harm-reduction measures that have proved effective in reducing blood-borne infectious disease in the case of heroin may also be important in minimizing the public health threat presented by outbreaks or transitory intensifications of amphetamine abuse.

See also **Epidemics of Drug Abuse in the United States; International Drug Supply Systems.**

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AMYGDALA. The amygdala, a region of the brain, is part of the limbic system. The limbic system is a group of similar brain structures related functionally. They provide the basis for emotion and motivated behaviors including reward-related events. The amygdala is located in the temporal lobe and consists of several different parts. It plays a role in various brain functions including epilepsy, emotion, learning and memory, and drug abuse.

In particular, the role of the extended amygdala has become an area of recent investigation. The extended amygdala refers to a group of brain structures that extend from the amygdala to the nucleus accumbens; these brain regions are believed to participate in the general reward circuitry of the brain. The mesolimbic dopamine system sends projections to the amygdala; these axons arise from the dopamine cells in the ventral tegmental area.

The amygdala has long been established as an important area mediating stimulus-reward associations. This behavior is believed to play an important role in the seeking and using of drugs of abuse, especially cocaine. An informative way to study drug abuse in animal models is through the self-administration of drugs that are abused by humans. Rats can be trained to self-administer cocaine, and then the experimenter can interfere with the neurochemical transmission in the amygdala in particular, modulating dopamine receptors and concentrations. The result of this manipulation is that the animals will increase or decrease their rate of administration of drugs. Thus, the amygdala makes a significant contribution to the study of cocaine-taking behavior.

The amygdala also contributes to the rewarding properties of ethanol. Studies have examined the effect of altering neurotransmission in the amygdala on ethanol self-administration. Similar to the findings reported for cocaine, modulation of the amygdala causes animals to change their rate of ethanol administration.

The amygdala is also involved in the effects of chronic drug exposure on the brain. Small changes in neurochemicals in the extended amygdala suggest that it may be mediating chronic drug action. These studies indicate that changes in the amygdala after long-term drug exposure may contribute to relapse.

Together, the amygdala and nucleus accumbens may be the main brain regions that underlie the brain changes associated with drug (particularly cocaine) addiction.

See also **Brain Structures and Drugs; Cocaine; Dopamine.**

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ANABOLIC STEROIDS. Anabolic steroids are synthetic versions of the naturally occurring male sex hormone, testosterone. They are more properly called anabolic-androgenic steroids (AASs), because they have both bodybuilding (anabolic) effects and masculinizing (androgenic) effects. The masculinizing effects of testosterone cause male characteristics to appear during puberty in boys, such as enlargement of the penis, hair growth on the face and pubic area, muscular development, and deepened voice. Females also produce natural testosterone, but ordinarily in much smaller amounts than males.

AASs are sometimes referred to simply as steroids. Steroid means only that a substance either resembles cholesterol in its chemical structure or is made from cholesterol in the body. Thus, AASs are one kind of steroid. (They are not to be confused with an entirely different group of steroids called corticosteroids—of which prednisone and cortisone are examples—which are commonly used to treat illnesses such as arthritis, colitis, and asthma. In contrast to anabolic steroids, corticosteroids can cause muscle tissue to be wasted.) AASs are also referred to as ergogenic drugs, which means performance-enhancing. Street or slang terms for AASs include "roids" and "juice."

Generic name	Representative brand names
Injectable testosterone esters[a]	
Testosterone cypionate	Depo-Testosterone (Slang name: Depo-T), Virlon IM
Testosterone enanthate	Delatestryl
Testosterone propionate	Testex, Oreton propionate
Other injectables	
Nandrolone decanoate	Deca-Durabolin (Slang names: Deca, Deca-D)
Nandrolone phenpropionate	Durabolin
Methenolone enanthate	Primobolan Depot
Veterinary injectables used by humans	
Trenbolone acetate	Finaject (Finajet) 30, Parabolan
Boldenone undecylenate	Equipoise
Stanozolol	Winstrol V
Pills (17-alkylated AASs)[b]	
Ethylestrenol	Maxibolan
Fluoxymesterone	Halotestin
Methandroslenolene	Dianabol (Slang names: D-bol, D-ball)
Methenolone	Primobolan
Methyltestosterone	Android (10 & 25), Metandren, Oreton Methyl, Testred, Virilon
Oxandrolone	Anavar
Oxymetholone	Adroyd, Anadrol-50
Oxymesterone	Oranabol
Stanozolol	Winstrol

[a]Least toxic to liver and cholesterol levels; cause estrogen levels to increase.
[b]Most toxic to liver and cholesterol levels.

Table 1. Anabolic steroids used by bodybuilders. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Soon after testosterone was first isolated and synthesized in the laboratory in 1935, a number of synthetics were created to be used as medicines. The synthetic forms were developed because natural testosterone did not work very long when given as a pill or injection (it is subject to rapid breakdown in the body). Bodybuilders may have begun using AASs to build muscle size and strength as early as the 1940s. Olympic athletes started to use these drugs in the 1950s. Most of this use went undetected, however, because the technology of drug testing did not allow reliable detection of AASs in the urine until the 1976 Olympic Games. Even so, anabolic steroids did not become a household word until Canadian sprinter Ben Johnson tested positive for AASs at the Seoul Olympic Games in 1988. In the same year, a study reported that 6.6 percent of American male high school seniors had tried AASs. This study made it clear that elite athletes were not the only ones taking these drugs. By 1991, AASs were added by federal law to the list of Schedule III of the Controlled Substances Act. Schedule III Controlled Substances are recognized to have value as prescribed medicines, but also have a potential for abuse that may lead to either low to moderate physical dependence or high psychological dependence. Table 1 lists the names of some AASs that bodybuilders have used. Hundreds of AASs have been synthesized, and more comprehensive lists exist (Wright & Cowart, 1990; Yesalis, 2000).

Two naturally occurring steroids, dehydroepiandrosterone (DHEA) and androstenedione, are used by the body to make testosterone and estrogen (Corrigan, 1999). The benefits and adverse effects of synthetic DHEA and androstenedione are mostly unknown, but they are commonly believed to have anabolic and androgenic effects. Unlike other AASs, DHEA and androstenedione are neither regulated by the Food and Drug Administration nor listed as controlled substances in the United States. DHEA has been sold over-the-counter as a nutritional supplement in the United States since 1994, even though the International Olympic Committee,

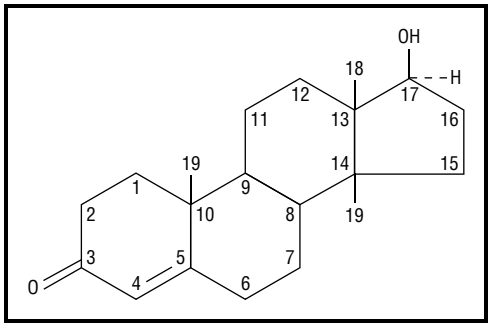

Figure 1. Testosterone molecule. The numbers refer to carbon atoms, and the hydrogen and hydroxyl groups are at carbon 17. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

many U.S. sports organizations, and some countries such as Australia ban it.

GENERAL CHEMICAL STRUCTURE

Testosterone has a four-ring structure composed of nineteen carbon atoms. Accordingly, the carbon atoms are labeled by number from one to nineteen (see Figure 1). Many synthetic forms of testosterone are made by adding either an alkyl group or an ester to the seventeen-carbon atom. An alkyl group is a chain of carbon and hydrogen atoms. An ester is formed by reacting an acidic chain of carbon and hydrogen atoms to the −OH group on the seventeen-carbon atom. In general, when an alkyl group is added to the seventeen-carbon atom, the resulting drug can be taken as a pill; however, these so-called seventeen-alkylated AASs are relatively toxic to the liver and are more likely to cause negative effects on cholesterol levels. By contrast, when an ester is formed at the seventeen-carbon atom, an injectable form of testosterone is created that is less toxic to the liver and cholesterol levels. Other AASs are created by making modifications at other carbon atoms.

MEDICAL AND NONMEDICAL USES

AASs are prescribed by physicians to treat a variety of medical conditions (Bagatell & Bremner, 1996). The most accepted use is for treating boys and men unable to produce normal levels of their own testosterone, a condition known as testosterone deficiency or hypogonadism. AASs are also used to treat a rare skin condition called hereditary angioedema, certain forms of anemia (deficiency of red blood cells), advanced breast cancer, and endometriosis (a painful condition in females in which tissue usually found only in the uterus develops in other body parts). AASs are also combined with female hormones to treat distressing symptoms that can accompany menopause. Experimentally, AASs have been used to treat a condition in which bone loss occurs (osteoporosis), to treat impotency and low sexual desire, and as a male birth control pill. In addition, AASs have been used in the treatment of Acquired Immune Deficiency Syndrome (AIDS) to stimulate appetite, weight gain, strength, and improvements in mood. Most of these medical uses are uncommon, either because the conditions are rare (such as angioedema) or because other treatments are preferred (such as erythropoeitin for anemia). Nevertheless, AASs are important medicines to have available.

Nonmedically, AASs are used to enhance athletic performance, physical appearance, and fighting ability. Since society endows people who look physically fit and attractive with many benefits and recognition, some individuals see AASs as a means to those benefits. Three groups of AAS users have been described:

1. The athlete group aims to win at any cost. The athlete also believes, sometimes correctly, that the competition is using AASs. The anticipated rewards to the athlete are the glory of victory, social recognition and popularity, and financial incentives (college scholarships, major league contracts).
2. The aesthete group aims to create a beautiful body, as if to make the body into a work of art. Aesthetes may be competitive bodybuilders, or aspiring models, actors, or dancers. They put their bodies on display to obtain admiration and financial rewards.
3. This group of AAS users seeks to enhance their ability to fight or intimidate. They include body guards, security guards, prison guards, police, soldiers, bouncers, and gang members. These people depend on fighting for their very survival.

Whether AASs actually work to improve performance and appearance has been debated.

Invariably, users believe AASs do work, but some scientific studies have failed to show an effect. However, there are serious limitations to how these studies were done and what they could show. In general, most researchers agree that AASs can work in some individuals to enhance muscle size and strength when combined with a proper exercise program and diet (Bagatell & Bremner, 1996; Bhasin et al., 1996). By contrast, AASs probably do not improve performance of aerobic or endurance activities (Yesalis, 2000).

CONSEQUENCES OF USE

AASs have been associated with a variety of undesirable effects. The most severe consequence attributed to their use is death. One study of mice given AASs revealed a shortened life span (National Institute on Drug Abuse, 2000). In humans, the distinction between fatalities that occur among relatively healthy athletes who use AASs and patients with illnesses (such as anemia) who are prescribed AASs is important, because ill patients are already at a higher risk for an early death. Nevertheless, reported deaths in nonmedical steroid users (such as athletes and aesthetes) have occurred from liver disease, cancer, heart attacks, strokes, and suicide (Yesalis, 2000; Pope & Brower, 2000). Clearly, anyone using AASs should have their health monitored by a physician.

Psychiatric Effects. Another serious, life-threatening consequence has been violent aggression toward other people. Both the medical literature and newspapers contain reports of previously mild-mannered individuals who committed murder and lesser assaults while taking AASs (Thiblin et al. 1997). Although reports of severe violence generate both alarm and widespread attention, the total number of such reports is small. Moreover, the effects of AASs on violent behavior vary widely depending on the social circumstances and the characteristics of the individual. Nevertheless, most but not all studies in humans have found that high doses of AASs increase feelings and thoughts of aggressiveness (Yesalis & Cowart, 1998). Although an increase in feelings and thoughts of violence does not always lead to violent behavior, it can be very distressing to the individual and to those around him or her. "Roid rage" is a slang expression used to describe the aggressive feelings, thoughts, and behaviors of AAS users.

Other psychiatric effects of AASs include mood swings and psychosis (Pope & Brower, 2000). AAS users commonly report that they feel energetic, confident, and even euphoric during a cycle of use. They may have a decreased need for sleep or find it difficult to sleep because of their high energy level. Such feelings may give way to feeling down, depressed, irritable, and tired between cycles of use. With continued use of high AAS doses, moods may shift suddenly, so that the user feels on top of the world one moment, irritable and aggressive the next, and then depressed or nervous. The appetite may also swing widely with cycles of use (Wright & Cowart, 1990). During a cycle on AASs, huge quantities of food may be consumed to support the body's requirements for muscle growth and energy. During the "off cycles," appetite may diminish.

The term *psychosis* means that a person cannot distinguish between what is real and what is not. For example, a person may believe that other people intend harm when no real threat exists; or a person may believe that an impossible, life-threatening stunt can be performed with no problem. Such false beliefs are called *delusions.* The psychotic person may also experience hallucinations, such as hearing a voice that is not there. Fortunately, most psychiatric effects of AASs tend to disappear soon after AASs are stopped, although a depressed mood may last for several months. Obviously, when suicides, homicides, or legal consequences from assault have occurred, they cannot be reversed simply by stopping one's use of AASs.

Effects on the Liver. AASs can affect the liver in various ways, but the seventeen-alkylated AASs are more toxic to the liver than other AASs. Most commonly, AASs cause the liver to release extra amounts of enzymes into the bloodstream that can be easily measured by a blood test. The liver enzymes usually return to normal levels when AASs are stopped. The liver also releases a substance called bilirubin, which in high amounts can cause the skin and eyes to turn yellow (a condition called jaundice). As many as 17 percent of patients treated with the seventeen-alkylated AASs develop jaundice (Yesalis, 2000). Nonmedical AAS users can also develop jaundice. Although untreated jaundice can be dangerous and even fatal, jaundice usually

disappears within several weeks of stopping AASs. Jaundice can also signal other dangerous conditions of the liver, such as hepatitis, so a physician should always treat it. Another condition that occurs among patients treated with AASs is peliosis hepatis, in which little sacs of blood form in the liver. Death can occur from bleeding if one of the sacs ruptures. Finally, liver tumors may occur in 1 to 3 percent of individuals (including athletes) using high doses of the seventeen-alkylated AASs for more than two years (Yesalis, 2000). Rare cases of liver tumors have been reported with other types of AASs as well. Some of the tumors are cancerous, and although more than half of the tumors disappeared when AASs were stopped, others resulted in death.

Potential to Affect the Heart. AASs can cause changes in cholesterol levels (Yesalis, 2000). Low amounts of a certain kind of cholesterol (high-density lipoprotein cholesterol) in the blood are known to increase the risk of heart attacks. AASs, especially the seventeen-alkylated ones, cause a lowering of this so-called good form of cholesterol. When AASs are stopped, however, cholesterol levels return to normal. Another risk factor for heart attacks and strokes is high blood pressure. Studies have shown that AASs can cause small increases in blood pressure, which return to normal when AASs are stopped. As a result of strenuous exercise, many athletes develop an enlarged heart that is not harmful. Some, but not all studies, suggest that AAS users can develop a harmful enlargement of the heart. As noted previously, heart attacks and strokes have been reported in AAS users, but studies are needed to determine if AAS users have a higher risk of heart attacks and strokes than nonusers (Yesalis, 2000).

Sexual Side Effects. AASs can alter the levels of several sex-related hormones in the body, resulting in many adverse effects (Wright & Cowart, 1990; Yesalis & Cowart, 1998). In males, the prostate gland can enlarge, making it difficult to urinate; the testes shrink; and sterility can occur. The effects on the prostate, the testes, and sterility reverse when AASs are stopped; however, at least one case of prostate cancer has been reported, an exception to reversibility. Males can also develop enlarged breast tissue from taking AASs, an effect medically termed *gynecomastia* (it is referred to by male users as "bitch tits"). Gynecomastia occurs because testosterone is chemically changed in the body to the female hormone, estrogen. Thus, the male user experiences higher amounts of estrogen than normal. Painful lumps in the male breast may persist after stopping AASs, and they sometimes require surgical removal. Females, however, may undergo shrinkage of their breasts, as a response to higher amounts of male hormone than normal. Menstrual periods become irregular and sterility can occur in females as well. Deepened voice and an enlarged clitoris are effects in females, which do not always reverse after stopping AASs. Women may also develop excessive hair growth in typically masculine patterns, such as on the chest and face. Finally, both males and females may experience increases and decreases in their desire for sex.

Other Effects. In children of both sexes before the onset of puberty, AASs can initiate the characteristics of male puberty and cause the bones to stop growing prematurely. The latter effect can result in shorter adult heights than would otherwise occur. AASs can cause premature baldness in some individuals, and it can cause acne. The acne is reversible with cessation of AASs. Other possible effects include small increases in the number of red blood cells, worsening of a condition called sleep apnea (in which afflicted persons stop breathing for short intervals during sleep), and worsening of muscle twitches (known as tics) in those who are predisposed.

Patterns of Illicit Use. AASs are commonly smuggled from countries where they are obtained over-the-counter without a prescription, and then sold illegally in the United States. Dealers and users typically connect in weight-lifting gyms. Users report that AASs are relatively easy to obtain.

Steroids are taken as pills, through skin patches, and by injection (Bagatell & Bremner, 1996). Injection occurs into large muscle groups (buttocks, thigh, or shoulder) or under the skin, but not into veins. Cases of acquired immune deficiency syndrome (AIDS) have been reported in steroid users due to needle sharing. Steroids are often taken in cycles of six to twelve weeks on the drugs, followed by six to twelve weeks off. At the beginning of a cycle, small doses are taken with the intent to build

to larger doses, which are then tapered at the end of a cycle. Illicit users typically consume ten to one hundred times the amounts ordinarily prescribed for medical purposes, requiring them to combine or "stack" multiple steroid drugs. The actual dose cannot always be determined, however, because illicit steroids may contain both falsely labeled and veterinary preparations. (Drugs purchased on the illicit market do not always contain what the labels indicate, and law-enforcement officials have confiscated vials contaminated with bacteria.)

Steroid users commonly take other drugs, each with their own risks, to manage the unpleasant side effects of steroids, to increase the body-building effects, and/or to avoid detection by urine testing (Wright & Cowart, 1990). For example, estrogen blockers, such as tamoxifen or clomiphene, are taken to prevent breast enlargement. Water pills (diuretics) are taken both to dilute the urine prior to drug testing and to eliminate fluid retention so that muscles will look more defined. Human chorionic gonadotropin (HCG) is an injectable, nonsteroidal hormone that stimulates the testicles to produce more testosterone and to prevent them from shrinking. Human growth hormone is another nonsteroidal hormone that is taken to increase muscle and body size.

Addictive Potential. As with other drugs of abuse, dependence on AASs occurs when a user reports several of the following symptoms: Inability to stop or cut down use, taking more drugs than intended, continued use despite having negative effects, tolerance, and withdrawal. "Tolerance" refers to needing more of a drug to get the same effect that was previously obtained with smaller doses, or of having diminished effects with the same dose. In terms of the anabolic effects, tolerance was demonstrated in animals in the 1950s. In recent studies, 12 to 18 percent of nonmedical AAS users reported tolerance (Yesalis, 2000; Copeland et al., 2000). Whether tolerance develops to the mood-altering effects of AASs is unknown. *Withdrawal* refers to the uncomfortable effects users experience when they stop taking AASs. As noted previously, many of the undesirable effects reverse when AASs are stopped, however, others can begin—such as depressed mood, fatigue, loss of appetite, difficulty sleeping, restlessness, decreased sex drive, headaches, muscle aches, and a desire for more AASs (Copeland et al., 2000). The depression can become so severe that suicidal thoughts occur. The risk of suicide described previously is thought to be highest during the withdrawal period.

Studies indicate that between 14 and 57 percent of nonmedical AAS users develop dependence on AASs (Yesalis, 2000), and rare cases have been reported in women (Copeland et al., 2000). These studies support the addition of AASs to the list of Schedule III controlled substances. Nevertheless, AASs may differ from other drugs of abuse in several ways. First, neither physical nor psychological dependence on AASs has been reported to occur when AASs are prescribed for treating medical conditions. This differentiates the AASs from the opioid pain killers and the sedative-hypnotics. Second, dependence may develop primarily to the muscle-altering effects of AASs, rather than the mood-altering effects. Some researchers have questioned whether AASs produce dependence at all, because most definitions of dependence require that drugs be taken primarily for their mood-altering effects. Third, AAS users appear more preoccupied with their bodies and how they look than do users of other drugs of dependence.

ANABOLIC STEROIDS: SUMMARY

The anabolic-androgenic steroids are related to the male sex hormone, testosterone. They have both masculinizing and bodybuilding effects. AASs are useful to treat a variety of mostly uncommon medical conditions. They are sometimes used for the nonmedical purposes of enhancing athletic performance and physical appearance. Most researchers agree with users that AASs can increase muscle size and strength in some individuals when combined with a proper exercise program and diet. Many are also concerned about the potential for harmful effects with AASs, especially when the patterns of illicit use are considered. Drugs obtained on the illicit market may be contaminated, falsely labeled, or may contain substances not approved for human use. Multiple steroid and nonsteroidal drugs are combined, and AAS doses may exceed therapeutic doses by ten to one hundred times. Although the seventeen-alkylated AASs are commonly used because pills are more convenient than injections, they are more toxic to the liver and cholesterol levels than the injectable testosterone esters. Nevertheless, injections carry their own risks

from improper injection techniques to dirty and shared needles.

The most serious side effects of AASs seem relatively uncommon, such as deaths or near-deaths from liver disease, heart attacks, strokes, cancer, suicide, and homicidal aggression. Most other side effects appear to be reversible when AASs are stopped, such as altered cholesterol levels, some liver effects, most psychiatric effects, testicular shrinkage, sterility, high blood pressure, and acne. Exceptions to reversibility include lumps in the male breast, deepened voice and enlarged clitoris in females, and cessation of bone growth in children. Moreover, some individuals may develop dependence on AASs, making it difficult for them to stop using. Stopping use can also produce distressing withdrawal symptoms, the worst of which is suicidal depression. Finally, studies of the long-term effects of using AASs are lacking, so safety cannot be assumed with the high-dose use of these drugs.

See also **Sport, Drugs in International.**

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ANALGESIC. Analgesics are drugs used to control pain without producing anesthesia or loss of consciousness. Analgesics vary in terms of their class, chemical composition, and strength. Mild analgesics, such as aspirin (e.g., Bayer, Bufferin), acetominophen (e.g., Tylenol), and ibuprofen (e.g., Advil), work throughout the body. More potent agents, including the opiates codeine and morphine, work within the central nervous system (the brain and spinal cord). The availability of the more potent analgesics is more carefully regulated than that of aspirin and other similar analgesic/anti-inflammatory agents that are sold in drugstores over-the-counter. The more potent opiate agents typically require prescriptions to be filled by pharmacists.

An important aspect of analgesics is that they work selectively on pain, but not on other types of sensation, such as touch. In this regard, they are easily distinguished from anesthetics that block all sensation. Local anesthetics, such as those used in dental work, make an area completely numb for several hours. General anesthetics typically are used to render patients unconscious for surgery.

See also **Pain, Drugs Used for.**

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ANHEDONIA. Anhedonia is the inability to derive pleasure from ordinary activities. Generally, certain stimuli (e.g., food, water, the company of

friends) serve as positive reinforcers in normal individuals. (*Positive reinforcement* is a descriptive term used by behavioral scientists to denote an increase in the probability of a behavior occurring in response to the presentation of a stimulus, such as food.)

Anhedonia may be idiopathic (of unknown cause), it may occur as a side effect of certain drugs (for example, the antipsychotic medications) that act as dopamine-receptor antagonists, or it may be an aspect of certain psychiatric disorders. Anecdotally associated with schizophrenia and postpsychotic depression, anhedonia is also associated with chronic unipolar depression, according to the *Diagnostic and Statistical Manual of Mental Disorders* (1994). It is also associated with drug dependence, a core symptom of which is the depression that occurs when the drug is no longer self-administered (Koob & Le Moal, 1997). The presence of anhedonia in chronic drug users is of considerable theoretical interest because it may give insight into the biological mechanisms that underlie drug dependence.

The acute administration of drugs of abuse elevates dopamine and serotonin levels in the nucleus accumbens, a brain structure that has been implicated in reinforcement. After the termination of drug use, dopamine and serotonin levels in the nucleus accumbens decrease below baseline levels, suggesting that this is the neurochemical basis for the associated anhedonia.

The hypothalamic-pituitary-adrenal (HPA) axis is another system that has been implicated in the anhedonia associated with drug withdrawal. The neuropeptide corticotropin-releasing factor (CRF) helps to regulate the HPA axis. CRF induces behavioral and physiological responses resembling those observed during exposure to stress, which includes the release of corticosteroids such as cortisol from the adrenal glands. Withdrawal from drugs of abuse such as cocaine, amphetamine, alcohol, and cannabinoids induces a strong activation of brain CRF systems, and antagonism of brain CRF receptors alleviates the negative affective symptoms associated with drug withdrawal (Koob, 1999). Chronic activation of the HPA axis may also lead to the development of anhedonia. This may explain why major depression is the most common comorbid psychiatric disorder in patients with Cushing's disease, which results from elevated systemic glucocorticoid levels.

See also **Brain Structures and Drugs; Depression; Dopamine; Physical Dependence; Reinforcement; Withdrawal.**

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ANORECTIC. This term derives from Greek (*a* + *oregein*, meaning "not to reach for"; later, *anorektos*) and it refers to a substance that reduces food intake. It came into use in English about 1900. Anorectic agents (also referred to as anorexics, anorexegenics, or appetite suppressants) fall into a number of categories according to the brain neurotransmitter system through which they work.

Central nervous system (CNS) stimulants that act through the noradrenergic and dopaminergic systems include cocaine, amphetamine-like compounds, mazindol, and phenylpropanalamine. Serotonergic compounds include fenfluramine, fluoxetine, and sertraline. Several endogenous peptides (within the body) also have anorectic actions, in that they inhibit food intake—these include cholecystokinin, glucagon, and the bombesin-like peptides.

Not *all* agents that can suppress appetite are medically approved for such use. For example, cocaine is approved *only* as a local anesthetic.

See also **Amphetamine.**

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ANOREXIA. *Anorexia* literally means "loss of appetite" and may be accompanied by moderate to extreme weight loss. People suffering from anorexia have little desire to eat, usually as a consequence of serious illness. It is often a symptom of depression and an accompaniment of alcohol and drug abuse, especially the abuse of cocaine and amphetamines. Anorexia should not be confused with anorexia nervosa, which is a mental illness with physical side effects akin to anorexia.

See also **Anorexia Nervosa; Bulimia Nervosa; Overeating and Other Excessive Behaviors.**

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ANOREXIA NERVOSA. Anorexia nervosa is a mental illness that is often accompanied by severe physical complications. Although the prevalence of anorexia nervosa among men may be rising, females are ten times more likely to receive this diagnosis than males. About 0.5 percent of young women are affected, with onset in late adolescence typical.

Anorectics frequently deny their illness, and many may otherwise appear well. Anorexia nervosa is characterized by deliberate weight loss, which is not explainable by disease or illness, and a refusal to maintain a healthy weight. It is accompanied by a distorted sense of body image and a fear of becoming fat regardless of current size or weight. Anorectics with the restricting subtype severely limit their diet by eating little food and/or food with low caloric content. Excessive exercise is also common. People with the bingeing and purging subtype may eat excessive amounts of food and engage in compensatory behavior, such as self-induced vomiting or misuse of diuretics and laxatives to alter the consequences of their perceived binge.

Including the term *anorexia* as part of the label for those with this disorder is somewhat misleading because those with anorexia nervosa purposefully deny themselves food in a misguided attempt to lose weight. Appetite is only lost after significant physical wasting occurs (i.e., muscles have degenerated).

Anorectics may develop a state of starvation that affects every major organ system in the body, especially the cardiac and electrolyte systems. People with this disorder also have thin, pale, inelastic skin; experience low blood pressure; feel cold all the time; lose hair on their head and sometimes grow body hair (lanugo) to conserve heat. The reproductive system is also affected with many women going through stages of amenorrhea (loss of three consecutive menstrual periods). As the most fatal of recognized mental illnesses, deaths occur in more than 10 percent of the anorectic population. Starvation, suicide, and electrolyte imbalance are among the leading causes of death for people with anorexia nervosa.

While the causes of anorexia nervosa are generally unknown, there are a few repeated patterns in the occurrence of the disorder. For example, anorexia is most commonly found in young women from industrialized countries, many of which promote unattainable standards of thinness through various kinds of media. In addition, the development of anorexia nervosa is genetically influenced, with altered neurobiology characteristic of both active and remitted phases of disorder. In general, anorectics tend to be perfectionistic, over-achievers of average or higher intelligence. They are also prone to depression and anxiety disorders. The bingeing and purging subtype tends to be impulsive and often has concurrent problems with alcohol and drug abuse, risky sexual behavior, and suicidal ideation and attempts.

Treatment for this disorder is twofold. The first objective is to restore weight and save life, which can require hospitalization. The second objective is to address the psychological issues contributing to

weight loss and the fixation on physical appearance as a basis for self-esteem.

See also **Anorexia; Bulimia Nervosa; Overeating and Other Excessive Behaviors.**

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ANSLINGER, HARRY JACOB, AND U.S. DRUG POLICY. For almost a third of a century, one man, Harry Jacob Anslinger (1892–1975), played the dominant role in shaping and enforcing U.S. drug policy. From 1930 to 1962, Anslinger served as Commissioner of the Federal Bureau of Narcotics (FBN, later Drug Enforcement Administration), which was housed in the U.S. Treasury Department. Only J. Edgar Hoover served a longer term in a federal appointed position. Anslinger also served as chief U.S. delegate to international drug agencies, including the United Nations, until 1970. He saw three major pieces of drug legislation through Congress, and much of his legacy remained current as of 2008. Therefore, to understand the evolution and state of federal drug policy, one must examine Anslinger's life and work.

Anslinger was born in Altoona, Pennsylvania, on May 20, 1892, the eighth of nine children in a Swiss immigrant family. In his book *The Murderers*, Anslinger wrote about an incident early in his life that shaped his ideas about narcotic drugs. At the age of twelve, he was sent to the drugstore by a neighbor to pick up a package of morphine for the neighbor's wife who was screaming in pain. Anslinger wrote: "I recall driving those horses, lashing at them, convinced that the woman would die if I did not get back in time. When I returned with the package—it was morphine—the man hurried upstairs to give the woman the dosage. In a little while, her screams stopped and a hush came over the house. I never forgot those screams. Nor did I forget that the morphine she had required was sold to a twelve-year-old boy, no questions asked" (Anslinger & Oursler, 1961).

About a decade after this incident, Congress passed the Harrison Narcotics Act of 1914, the first federal law against selling or using narcotics. Prior to that, narcotics were inexpensive, and many people used them as legal painkillers. Some people became addicted, often without realizing it, maintaining a steady dosage of cheap drugs that enabled them to manage their pain and continue to function satisfactorily at work and at home.

At age fourteen, Anslinger started working for the Pennsylvania Railroad while taking high school courses in his free hours. Without a high school diploma, he entered Pennsylvania State College in 1913 and completed a two-year program in engineering and business management. He continued to work part-time and summers for the railroad and played the piano for silent movies.

During summer break from Penn State, a very young Anslinger was exposed to a second incident that would shape his life—this one involved a fellow Pennsylvania Railroad worker, an immigrant named Giovanni, whom Anslinger found shot and beaten alongside the railroad tracks. Anslinger suspected that the hard-working, humble Giovanni was the victim of an extortionist working for the so-called Black Hand (*Mano Nero* in Italian). Giovanni survived the attack, and Anslinger questioned him while he was recovering in the hospital. After guaranteeing Giovanni that his family would be safe, Anslinger learned that Big Mouth Sam was the perpetrator. Anslinger found Big Mouth Sam and greeted him with "I'm Giovanni's boss and friend." In *The Murderers*, Anslinger wrote: "I told him I knew he was the one who pumped all that le[a]d into Giovanni's body and dumped him in the ditch. 'If Giovanni dies,' I warned him, 'I'm going to see to it that you hang. Do you understand that?' Big Mouth started to object again but I cut him short. 'And if he lives and you ever bother him again, or any of my men, or try to shake any of them down any more, I'll kill you with my own hands.'" Anslinger concluded, "Such was my first direct encounter with this transplanted

Anslinger helped create the 1931 Narcotics Limitations Convention, which regulated the production of drugs for medical uses. AP IMAGES

brotherhood of plunder, extortion, thievery and murder" (Anslinger & Oursler, 1961, p. 10). Throughout his career, Anslinger kept a sharp eye on underworld-type characters, effecting many of their arrests because of drug smuggling.

In 1917, Anslinger volunteered to help the American effort in World War I and worked for the U.S. Army as assistant to the chief of inspection of equipment. In 1918, Anslinger entered the U.S diplomatic service. He spoke fluent Dutch and German, and his first post, which lasted three years, was the Netherlands, where he was assigned as liaison to the entourage of deposed Kaiser Wilhelm. In summer 1921, he was sent to Hamburg, Germany, and in 1923, he was reassigned from Germany to Venezuela for a frustratingly dull three-year tour as U.S. vice consul in LaGuaira, the port for the capital city of Caracas.

FEDERAL BUREAU OF NARCOTICS

In 1920, the Prohibition Amendment made importing, manufacturing, or selling alcoholic beverages illegal throughout the United States and its possessions. People with sacramental or medicinal needs could possess a small amount of alcohol. History clearly shows that illegal liquor became an instant success. In 1926, Anslinger became U.S. consul in Nassau in the British Bahamas, at the time a principal source from which illegal alcohol was smuggled into the United States. Consul Anslinger was quickly recognized for his effective work in persuading the British authorities to cooperate in curbing the flow of alcohol. The Volstead Act (1919) and the Harrison Act (1914), which were aimed respectively at enforcing Prohibition and controlling the distribution of narcotic drugs, were both tax measures under the jurisdiction of the Treasury Department. The U.S. Treasury soon borrowed Anslinger from the Department of State to serve in its Prohibition Unit, which then enforced both acts. The Narcotics Division of the Prohibition Unit was headed from 1920 to 1930 by Colonel Levi G. Nutt. However, Nutt was fired in 1930 after a 1929 investigation revealed misconduct in his office, which he denied. On July 1, 1930, three years before Prohibition ended, the drug-regulation functions were shifted to a new Federal Bureau of Narcotics (FBN), and on September 23, 1930, President Herbert C. Hoover appointed Anslinger its first Commissioner.

Immediately, Anslinger began what would be an important part of his legacy: He espoused the notion that the threat of punitive measures would deter drug traffickers and users. So for thirty-plus years, Anslinger claimed that higher fines and longer prison terms were the best corrective action for the increasing narcotic drug-use problem in the United States.

Because the Harrison Act was passed as a revenue measure, individual states had to legislate prohibition and penalties. So through the 1920s, almost every state created narcotic control laws. However, by 1930, some leaders in government, medicine, and pharmaceuticals began to urge passage of a federal law for a few reasons: The states' laws were very uneven, states did not have the support and resources to effectively curb drug trafficking, and the media were beginning to report on drug addiction, planting the seed for ensuing hysteria around drug addicts.

Anslinger and the FBN promoted passage of the Uniform State Narcotic Drug Act, mostly because it kept out of their jurisdiction the so-called nuisance drug marijuana. A voracious reader, Anslinger probably was aware of the National Wholesale Druggists' Association's position that cannabis should not be included in any federal legislation because it "was not what might be called a habit-forming drug" (Musto, 1987, p. 217). Anslinger knew that cramming the courts with marijuana cases would cast an unfavorable judicial light on the Bureau, so he instructed his agents to police more lethal drugs, cocaine, and opiates. Yet during his tenure as commissioner, Anslinger dominated the enactment of U.S. narcotics laws.

MARIJUANA TAX ACT OF 1937

Supporting the Uniform State Narcotic Drug Act, Anslinger almost never mentioned marijuana during the first half of the 1930s. However, in 1936, F. W. Russe, secretary of Mallinckrodt Chemical Works, wrote to Anslinger asking whether the news he had heard about a bill titled the Secret Service Reorganization Act was accurate. The act would collapse a number of federal bureaus into one, and the FBN was among them. Thus, Anslinger could have been forced out of his position, and the FBN diluted.

At that moment, Anslinger found the argument that he would pull out every time he wanted stronger narcotics-abuse penalties: the threat of marijuana corrupting the nation's youth. At that time, marijuana (*Cannabis sativa*) had limited favor among a few Caribbean Blacks, Hispanic Americans, and jazz musicians. A number of responsible studies of the effects of marijuana (such as one by the Hemp Commission in British India in 1985) and its more potent form, hashish, had pronounced the drug relatively harmless. Evidence in Anslinger's personal files shows that he was aware of such studies (Anslinger Papers). However, to promote the so-called marijuana-menace scare, Anslinger related shocking accounts of heinous crimes induced by marijuana, and he introduced the theory that smoking marijuana was a dangerous gateway to other more serious addictions. His cause received a boost from the originally church-sponsored-now-cult film *Reefer Madness*, a morality tale that popularized Anslinger's visions of the hazards of drug use. As a result, the Reorganization Act was abandoned. Anslinger's Bureau was saved.

Yet Anslinger's campaign to save the Bureau brought the topic of marijuana much more into the media, and because many groups clamored for protection against dope fiends, Anslinger agreed to help draft the Marijuana Tax Act, placing marijuana in the same highly restricted category as heroin and cocaine. President Franklin Delano Roosevelt signed the bill on August 2, 1927. Research on its toxic properties was stifled because the FBN would not license its use by researchers outside of government. Although its therapeutic value in alleviating nausea due to chemotherapy for cancer patients or for treating glaucoma came to be generally recognized, the drug remained a Schedule One narcotic.

BOGGS ACT OF 1951

In the late 1940s, Anslinger claimed that the drug problem was caused by judges imposing lenient sentences on drug offenders. Anslinger's supporters in Congress picked up the argument, and the resulting legislation, the Boggs Act of 1951, increased the ten-year maximum sentence for drug offenders to a two-to-five-year sentence for first offenders, a mandatory five-to-ten-year sentence for second offenders, and a mandatory twenty-year sentence for third offenders; second and third offenders had no chance of probation or parole. When the act passed through Congress with almost no debate and no objection, Senator Estes Kefauver quoted Anslinger, referring to the increased penalties, saying, "I think it would just about dry up the traffic" (Congressional Record, October 20, 1951, 82nd Congress, 1st Session, 97: 13675). Narcotics traffic did not "dry up."

NARCOTICS CONTROL ACT

On November 3, 1951, the *New York Times* reported that President Truman had signed the Boggs Act and that the Veterans of Foreign Wars voted to "urge stronger state narcotics laws, with stiffer penalties for offenders," including "the death penalty for persons selling narcotics to teenagers." Thus, the quest for even stronger penalties was to continue.

The November 23, 1953, the *Washington Post* ran this headline: "Anslinger Asks Senate Action on Addict Bill; Hospitalization Law Still Needed, He Says; Drug Use Declines." And his hometown newspaper, which reported on him regularly, ran this headline: "Anslinger Calls for Stiffer Penalties on Dope Peddlers to Protect Youth of Nation." Both articles reported on Anslinger's testimony before the Senate Juvenile Delinquency Subcommittee, during which he called for stiffer state and federal penalties against drug peddlers to help break up the rings of racketeers preying on the nation's youth.

Anslinger never wavered from this position, despite the expert opinion of, among others, sociologist Alfred R. Lindesmith, who claimed that the prohibition control technique and the "complete removal of the control issue from the medical domain" were the causes of the country's addiction problems (Lindesmith, 1956). Lindesmith narrowed the problem to "non-addicted lords of the underworld" as the "focal point of the new infection." He added, "These men [the non-addicted bosses] are rarely apprehended or punished; it is the user, exploited by the system, who suffers the major portion of the heavy penalties that are imposed." And he pointed out that "police suppression, by increasing the danger of distribution and reducing supplies, keeps up prices and profits,"

thus keeping the illicit market alive, drug lords safe, and addicts facing prison.

The *New York Times* covered Anslinger's testimony in a June 3, 1955, article, quoting him as claiming that the nation's failure to curb drug addiction lay primarily with "the legislators and other officials" who had been lax in creating and enforcing stringent narcotics laws. Congresspersons reacted to Anslinger's testimony with a groundswell of bills for narcotics legislation with even stiffer penalties.

On April 30, 1956, the Daniel subcommittee presented findings and recommendations that Anslinger himself could have written. It drafted Senate Bill 3760, and on May 15, 1956, the Senate Judiciary Committee unanimously approved the bill. When President Eisenhower signed the Narcotic Control Act on July 18, 1956, he put into place the heaviest penalties for U.S. narcotics law violations to that date.

Three months later, probably not coincidentally, Senator Price Daniel announced his bid for governor of Texas (and received praise from the *New York Times* for his work on the Senate Juvenile Delinquency Subcommittee, saying that its early completion was "unusual . . . in the run of Congressional investigations").

This rash of bills introduced in Congress demonstrates one of the more evident results of Anslinger's tenure: Elected officials rallied behind him and his notion of demon drug addicts corrupting the nation's young people. Protecting the nation's youth was a sure ticket to re-election. This worked well for Anslinger, despite an even more extensive study performed by a joint committee of the American Bar Association and the American Medical Association on which Rufus King served—King, the original author of this entry—as it gave Anslinger strong support in Congress (King 1974).

INTERNATIONAL DRUG POLICIES

By 1930, when Anslinger became commissioner, the patterns of international controls had also been largely set, with the United States urging stringent repression and most of the rest of the world remaining indifferent or resistant. (The basic Hague Convention of 1912 would not have been ratified by more than a few nations had not the United States insisted upon its inclusion in the Paris peace treaties, which created the League of Nations in 1921.) Although the United States never joined the League of Nations, U.S. representatives were given a voice in drug matters, and Anslinger dominated international deliberations, leading the U.S. delegations first to the drug-control agencies of the League of Nations and then to those of the United Nations even after his resignation as FBN commissioner.

Anslinger participated in drafting the 1931 Narcotics Limitation Convention, which imposed controls on the production of drugs for legitimate medical uses; he pressed for the 1936 Convention for Suppression of Illicit Traffic, which sought to persuade other nations to impose criminal sanctions on domestic distribution and consumption. When World War II isolated Geneva and ended most of the functions of the League of Nations based there, he arranged for moving the international drug agencies to New York City, where they continued to operate. After the war, he was the leading proponent of a Single Convention, finally approved in 1961, after ten years of drafting. It incorporated much of the U.S. law-enforcement orientations, including obligations upon members to control crops and production, to standardize identification and packaging, and to impose severe criminal penalties on drug offenders. But lacking enforcement sanctions, the Single Convention had little effect.

AFTER FBN: ANSLINGER'S LEGACY

Some reports say that Anslinger was forced out of the FBN by the Kennedy administration. More reliable evidence says he was not. In fact, he offered his resignation on his seventieth birthday, May 20, 1962, but the Kennedy administration asked him to remain as acting commissioner until a successor could be found. He did so and was pleased when his closest aide, Deputy Commissioner Henry L. Giordano, was appointed by President Kennedy as the new commissioner and promised that he would make no changes in policies established by Anslinger. And he did not. In fact, in 1967, Giordano was still presenting exaggerated marijuana claims in his testimony before the U.S. Congress, reminiscent of Anslinger's 1930's testimony (Treasury-Post Office Departments and Executive Office Appropriations, Hearings, before a subcommittee of

the Committee on Appropriations, 90th Cong., 1st sess., 1967, 404–485).

Kennedy also permitted Anslinger to remain as U.S. representative to the United Nations, a post he held until 1970. Anslinger, for his part, praised Attorney General Robert Kennedy, the president's younger brother, for pursuing top figures in the Mafia, not merely jailing addicts. After the Kennedy assassination in 1963, President Lyndon B. Johnson moved much of the federal drug-control apparatus from the Treasury Department to the Department of Justice.

Anslinger retired to his home in Altoona, Pennsylvania, and died in 1975. He donated his papers to Pattee Library (later Paterno Library) at the Pennsylvania State University (PSU), University Park, Pennsylvania. The thirteen boxes are housed in the Historical Collections and Labor Archives (Accession 1959-0006H).

Anslinger's legacy lives on. Presidents Nixon (1969–1974), Reagan (1981–1989), and George H. W. Bush (1989–1993) intensified the drug war, justifying such efforts with arguments initially developed by Anslinger. Congress, too, continued to be influenced by Anslinger's views. Congressional speeches and penal statutes continue to be extreme and racially biased. Marijuana is still a Schedule One narcotic, grouped with heroin and cocaine.

In hindsight, a three-pronged approach to narcotics—punishment for importing and selling drugs, medical treatment for addicts, and honest education about the facts of drug use—sounds like sensible drug policy that could have benefited the United States since the 1930s. Anslinger's detractors call him evil, which is probably too strong. However, he was overzealous and a product of his upbringing. He had seen the pain that addiction caused his neighbor's wife. He had seen the evil of organized crime. He had seen decisive American military force in World War I destroy the empires of Germany and Austria-Hungary. He had seen the Allies fight crime and exact severe punishment. He wanted to fight the evil of drug addiction. The solution seemed simple: make everything connected with narcotics—sale, use, importation, manufacture—illegal. Lock up everyone involved in any way with any drug for as long as possible. He seems not to have realized that his extreme criminalization policies created a niche for international criminals to fill and little-to-no recourse for medical doctors and addicts to legally attempt to cure reliance on narcotic drugs. The punitive over medical approach, Anslinger's greatest legacy, continues.

See also **Prohibition of Alcohol.**

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ANTAGONIST. An antagonist is a drug that binds to a receptor (i.e., it has affinity for the receptor binding site) but does not activate the receptor to produce a biological response (i.e., it possesses no intrinsic activity). Antagonists are also called receptor "blockers" because they block the effect of agonists. The pharmacological effects of an antagonist therefore result in preventing agonists (e.g., drugs, hormones, neurotransmitters) from binding to and activating the receptor. A competitive antagonist competes with an agonist for binding to the receptor. As the concentration of antagonist is increased, the binding of the agonist is progressively inhibited, resulting in a decrease in the physiological response. High antagonist concentrations can completely inhibit the response. This inhibition can be reversed, however, by increasing the concentration of the agonist, since the agonist and antagonist compete for binding to the receptor. A competitive antagonist, therefore, shifts the dose-response relationship for the agonist to the right, so that an increased concentration of the agonist in the presence of a competitive antagonist is required to produce the same biological response observed in the absence of the antagonist.

A second type of receptor antagonist is an irreversible antagonist. In this case, the binding of the antagonist to the receptor (its affinity) may be so strong that the receptor is unavailable for binding by the agonist. Other irreversible antagonists actually form chemical bonds (e.g., covalent bonds) with the receptor. In either case, if the concentration of the irreversible antagonist is high enough, the number of receptors remaining that are available for agonist binding may be so low that a maximum biological response cannot be achieved even in the presence of high concentrations of the agonist.

See also **Agonist; Agonist-Antagonist (Mixed); Antagonists of Alcohol and Drugs; Naloxone; Naltrexone.**

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ANTAGONISTS OF ALCOHOL AND DRUGS. Pharmacologic antagonists are medications designed to counteract the effects of another drug. Most drugs of abuse exert their effect on the central nervous system (CNS) by binding to a specific chemical receptor in the brain where they mimic the actions of endogenous (natural) neurotransmitters. Therefore, they are pharmacologic agonists (i.e., they mimic the action) at that particular neuronal receptor or binding site. Pharmacologic antagonists work against the agonist by preventing the drug effect.

Generally, the antagonist is chemically similar enough to the agonist to fit into the receptor site but dissimilar enough to exert little or no pharmacologic action. Instead, the antagonist occupies the receptor site, preventing the agonist drug from binding to the site and exerting its action, which is called a *competitive antagonism*. In addition to pharmacologic antagonists, another group of drugs useful in the treatment of addiction are the *partial agonists*, which act as weak agonists at the receptor site while blocking the effects of the drug of abuse. One way to understand this phenomenon is to think of the receptor site as a lock and the endogenous neurotransmitter as the master key. The agonist drug acts as a duplicate key, similar enough to the master key to open the lock, whereas the antagonist key is similar enough to the master key to fit into the lock but dissimilar enough not to open the lock but instead to jam it. The partial agonist can open the lock with some effort, but often, the key will stick.

Pharmacologic antagonists can be used to treat both the immediate and long-term effects

of drugs of abuse. For example, overdose, either intentional, as in a suicide attempt, or unintentional, as occurs when a street drug of unknown potency is used, is one of the most serious consequences of drug abuse. In addition to the usual supportive emergency care that is given to patients when they are brought into the hospital, pharmacologic antagonists of drugs of abuse can be administered to counteract directly the dangerous effects of these drugs. Pharmacologic antagonists may also be used preventively, to decrease craving and prevent relapse in individuals who are addicted to an agonist drug. This entry reviews the most commonly used pharmacologic antagonists of alcohol and other drugs of abuse.

NALOXONE

Naloxone (Narcan) is an injectable opiate antagonist used to reverse the severe respiratory depression induced by an opiate overdose, such as heroin can cause. It is also used in certain therapeutic situations such as when the effect of a narcotic given for legitimate medical reasons must be reversed (e.g., following surgery during which opiates are used during anesthesia). Sometimes naloxone is given in an emergency situation in order to confirm a suspected opiate overdose. Naloxone can also be employed to diagnose chronic opiate abuse, but in most cases narcotics can be detected by standard laboratory testing without the risk of inducing sudden withdrawal symptoms, as occurs when an opiate-dependent person is administered an opiate antagonist. In the event of an opiate overdose, naloxone should be used in the context of other supportive medical care, including the administration of CPR, oxygen, and mechanical ventilation, as may be required given the severity of the overdose. The abrupt return to consciousness that naloxone induces in overdose patients can be jarring, causing tremor and hyperventilation. Naloxone administered too rapidly or in too high a dose can precipitate withdrawal symptoms, including nausea, vomiting, tachycardia (rapid heartbeat), and sweating. Since the half-life of naloxone is generally less than two hours and that of many opiates considerably longer, the drug must be given by continuous intravenous infusion for a least a day following the acute overdose.

FLUMAZENIL

Flumazenil (Romazicon) was developed as an aid to the management of benzodiazepine (e.g., Valium) overdose. It also reverses the effects of benzodiazepines used for the induction and maintenance of anesthesia. Flumazenil works at the benzodiazepine receptor site in the brain, also known as the GABA/benzodiazepine receptor complex, where it displaces the benzodiazepine from the binding site. Flumazenil works quickly; when injected, its effects can be seen within one to two minutes. However, since the half-life of the drug is only about one hour and that of many benzodiazepines is considerably longer, multiple injections may need to be given. In an overdose situation, flumazenil is considered to be an adjunct to, rather than a replacement for, conventional supportive care. In clinical studies, 80 percent of patients admitted to the hospital with a benzodiazepine overdose responded to flumazenil with an improvement in their level of consciousness.

There is considerable controversy over the use of flumazenil in a patient who has overdosed, either intentionally or not. Benzodiazepine overdose alone is rarely fatal. If the patient has taken only a benzodiazepine, chances are good that he or she will wake up once the drug wears off, with or without an antagonist. In the case of a mixed overdose, such as when a patient takes amphetamines or certain kinds of antidepressants along with the benzodiazepine, the benzodiazepine could actually have the therapeutic effect of preventing seizures in these individuals. Administering flumazenil could actually induce dangerous seizures in this situation. Reversing the sedating effects of the benzodiazepine rapidly can also cause agitation or anxiety. In clinical studies, up to 3 percent of patients treated with flumazenil required treatment for anxiety or agitation. Flumazenil may be best used in situations when benzodiazepines are taken in combination with other depressants (i.e., downers) such as alcohol because the combination of multiple central nervous system (CNS) depressants can be fatal. Flumazenil can also be useful in some cases as a diagnostic tool: If the antagonist revives an unresponsive patient, the likelihood that other CNS depressants are present is lower.

NALTREXONE

Naltrexone (Revia, Vivitrol), an opiate antagonist, was first introduced for the treatment of opiate

dependence, but it is used most often for the treatment of alcohol dependence. Although chemically similar to naloxone, naltrexone was synthesized to be an effective opiate antagonist that could be administered orally. (In contrast, naloxone is destroyed in the gastrointestinal tract when taken by mouth.)

Naltrexone has a high affinity for the μ opiate receptor, which has been implicated in the development of alcohol dependence. The exact mechanism by which naltrexone reduces the risk of heavy drinking is not known, but studies suggest that alcohol stimulates the release of endogenous opiate agonists and that naltrexone then blocks these natural opiates, making alcohol consumption less rewarding.

Naltrexone was originally available only in tablet form, but in 2006 a long-acting injection formulation (Vivitrol) was introduced. This extended release suspension is injected once a month into the gluteal muscle of the buttock. The drug is then released slowly from this site over the course of a month. Long-acting naltrexone has an important advantage over oral naltrexone: For each month that the patient receives an injection, there is no risk of the patient either forgetting a dose or choosing not to take a dose. Naltrexone is not approved by the Food and Drug Administration for the treatment of patients who are actively drinking, but rather for the prevention of relapse and as an adjunct to psychotherapy in individuals who have already demonstrated an ability to abstain from alcohol outside an institutional setting. The most common side effects associated with naltrexone are nausea and headache; patients who receive the long-acting formulation often experience discomfort at the site of the injection. Although liver toxicity has not been reported at the approved dosage, naltrexone has been reported to cause liver damage at five times the therapeutic dose. This adverse effect is an important consideration for alcohol-dependent patients, however, since some may already have alcohol-related liver disease.

BUPRENORPHINE AND NALOXONE

Buprenorphine (Suboxone, Subutex) is a partial μ opiate receptor agonist and a K opiate receptor antagonist that is used both for the treatment of pain and for the treatment of opiate dependence. Buprenorphine is chemically similar to other opiates such as morphine, codeine, and heroin, but it produces less euphoria (drug high) than these agents. When used for the treatment of opiate dependence, buprenorphine is initially given in a sublingual fixed-dose combination tablet with the opiate antagonist naloxone (Suboxone). The presence of the naloxone in the tablet is intended to prevent abuse of the buprenorphine; when the medication is taken correctly (dissolved under the tongue), the buprenorphine is absorbed directly into the bloodstream, avoiding metabolism by the liver while the naloxone is only minimally absorbed by this route and thus exerts only a minimal pharmacologic effect. If the patient attempts to abuse the medication by dissolving the tablets and injecting them into the bloodstream, the naloxone will have full pharmacologic effect and induce withdrawal symptoms. A second formulation of buprenorphine (Subutex) does not include naloxone.

Buprenorphine, like methadone, is used for the treatment of opiate dependence, but unlike methadone, use of buprenorphine is not limited to being dispensed in a clinic. The Drug Addiction Treatment Act (DATA) of 2000 allows physicians who meet certain requirements to treat a limited number of dependent patients with buprenorphine in their office practice. In a study of 326 opiate-addicted persons treated in a physician's office, 18 percent of subjects assigned to treatment with buprenorphine, and 21 percent of subjects assigned to treatment with buprenorphine and naloxone achieved a *clean* urine compared with only 6 percent of those randomized to placebo. The dependent patient is first treated at the doctor's office with buprenorphine alone (Subutex), titrated (measured for strength) to an effective dose over a period of two days, and then transferred to the combination product (Suboxone). Pharmacists filling prescriptions for buprenorphine and naloxone tablets are required by law to verify both that the physician is certified to write for the medication and that the prescription is legitimate (i.e., not a forgery). The most common adverse effects of buprenorphine are sedation, nausea, hypotension (decreased blood pressure), respiratory depression, and diaphoresis (sweating). Patients may also become physically or psychologically dependent on buprenorphine, but the intensity of this dependence is less severe than with other opiates.

VARENICLINE

Varenicline (Chantix), an aid to smoking cessation, was introduced in 2006. It is a partial agonist of the $\alpha 4\beta 2$ nicotinic receptor, which is believed to mediate the addicting effects of nicotine. Varenicline both blocks the effects of nicotine and acts as a mild agonist; that is, it stimulates the nicotine receptor, but at a much lower level than nicotine. Varenicline is taken orally and is intended to be used in combination with psychosocial support. The dose of the drug is titrated upward over a period of eight days and then given over a 12-week period. Patients who are able to stop smoking should continue the medication for another 12 weeks to decrease the likelihood of relapse. Not everyone who takes varenicline is able to quit smoking, but in clinical trials, varenicline was significantly more effective than bupropion (Zyban), another non-nicotine drug used to treat nicotine addiction. In one study, 44 percent of patients assigned to varenicline were able to stop smoking, compared to 30 percent of those assigned to bupropion and only 17 percent of those assigned to placebo (an inactive medication).

The most common side effects with varenicline are nausea, vomiting, sleep disturbance (vivid or abnormal dreams), constipation, and flatulence (gas). Varenicline can also cause serious psychiatric effects, most significantly depression and even suicide. Although these effects are not common, given their severity, physicians are advised to monitor all patients taking varenicline for changes in behavior and mood. Patients are also advised to contact their physician if they experience agitation, depressed mood, behavior changes, or suicidal thoughts.

See also **Treatment: An Overview of Alcohol Abuse/Dependence; Treatment, Pharmacological Approaches to: Methadone; Treatment, Pharmacological Approaches to: Naltrexone.**

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ANTIDEPRESSANTS.

See **Treatment, Pharmacological Approaches to: Antidepressants.**

ANTIDOTE.

A medication or treatment that counteracts a poison or its effects. An antidote may work by reducing or blocking the absorption of a poison from the stomach. It might counteract its effects directly, as in taking something to neutralize an acid. Or an antidote might work by blocking a poison at its receptor site. For example, a medication called *naloxone* will block opiates such as heroin at its receptors and prevent deaths that occur because of heroin overdose. In a sense, drug antagonists can all be antidotes under some circumstances, but not all antidotes are drug antagonists.

Many cities have a telephone "poison hot line," where information on antidotes is given. In case of drug overdose or poisoning, it is advisable to call for expert medical help immediately.

See also **Antagonist; Poison.**

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ANTISOCIAL PERSONALITY DISORDER.

Antisocial personality disorder (ASPD) is particularly germane to alcohol and drug use disorders (A/DUD) because it co-occurs in a large proportion of those with A/DUD, and it confounds the diagnosis of, influences the course of, and is an independent risk factor for the development of A/DUD. ASPD when comorbid with an A/DUD may also be more heritable than ASPD alone.

DSM-IV DIAGNOSIS WITH CONDUCT DISORDER

Using the diagnostic criteria of the *DSM-IV*, the diagnostic classification system published by the American Psychiatric Association and in widespread use, ASPD is defined as a disorder characterized by general disregard for and violation of the rights of others that begins in childhood or early adolescence and continues into adulthood. To receive a diagnosis of ASPD, the individual must be at least eighteen years old and have a history of conduct disorder.

The diagnosis of conduct disorder requires that at least three of the following behaviors must have occurred in any twelve-month period of time before the age of fifteen (or age thirteen for some behaviors): running away from home overnight at least twice (or once without returning); staying out late contrary to parental rules (beginning before age thirteen); repeated truancy (beginning before age thirteen); initiating physical fights; using weapons; cruelty to animals or to people; forcing someone into sexual activity; frequent bullying; robbing, or mugging someone; arson; vandalism; frequent lying to obtain favors or goods; breaking into someone's house or car; and stealing.

In addition, three of the following behaviors must have occurred since the age of fifteen: consistent irresponsibility; failure to conform to social norms; irritability and aggressiveness; deceitfulness; reckless disregard for safety of oneself or of others; impulsivity or failure to plan ahead; and lack of remorse for hurtful or manipulative behaviors. *DSM-IV* acknowledges but does not recognize as a full disorder a syndrome of adult antisocial behavior without the childhood component (Adult Antisocial Behavior Syndrome, AABS). Individuals with AABS are similar to their ASPD counterparts on adult antisocial behavior, drinking and drug use history, and other psychiatric comorbidity.

ICD-10 WITHOUT CONDUCT DISORDER

Conceptualization of ASPD differs in the diagnostic classification system formulated and published by the World Health Organization, the *International Classification of Diseases* (*ICD-10*). In that system, ASPD is termed *dissocial personality disorder* (DPD) and does not require the presence of conduct disorder, although some of the dissocial behaviors must have occurred early in life. To meet criteria for DPD, an individual must have three of the following persistent behaviors: callous unconcern for the feeling of others; gross irresponsibility and disregard for social norms; incapacity to maintain enduring relationships; incapacity to experience guilt and benefit from experience; low tolerance for frustration and low threshold for aggression; and marked proneness to blame others for the dissocial behavior. The *ICD-10* diagnosis of DPD is, therefore, more severe than the *DSM-IV* diagnosis of ASPD.

A large percentage of those with A/DUD meet criteria for ASPD. Data from a 2001–2002 survey of 43,000 adults eighteen or older in the U.S. general population showed that among those with a lifetime history of any *DSM-IV* alcohol use disorder (AUD), 10.4 percent of men and 6.6 percent of women (compared with 5.5 percent of men and 1.9 percent of women overall) had a diagnosis of ASPD, and, combining ASPD and AABS, 39.4 percent of men and 34.0 percent of women had any antisocial behavior syndrome (ASB). Among those with drug use disorders (DUD), the prevalence estimates were even greater: 20.7 percent of men and 14.1 percent of women had ASPD, and 44.0 percent of men and 39.0 percent of women had AABS.

The reverse associations are also true. Three times as many men with ASPD as without meet lifetime criteria for AUD, and five times as many men with ASPD as without meet criteria for DUD. The associations are even stronger among women, with twelve times as many women with ASPD as without meeting criteria for AUD and thirteen times as many meeting criteria for DUD.

THERAPIES AND TREATMENT

ASPD affects the course of A/DUD. Individuals with A/DUD complicated by ASPD have a more chronic and severe course, including an earlier age of alcohol/drug initiation, greater quantity and frequency of use, and higher number of lifetime substance use problems. Furthermore, evidence indicates that although ASPD alcoholics are more likely to enter treatment than alcoholics without ASPD, they have a poorer response to treatment, relapsing much earlier than alcoholics without ASPD, and may respond only to certain therapies. For instance, psychotherapies designed to increase motivation (e.g., motivational enhancement therapy; MET) or to link behaviors and misperceptions to consequences (e.g., cognitive behavioral therapy; CBT) have been shown to have only modest efficacy. Twelve-step facilitation (TSF) has also been only somewhat helpful. Studies have not been consistent, however, in determining which treatment option is particularly efficacious for those with A/DUD comorbid with ASPD. Evidence from studies performed in the 1990s and early part of this century is equivocal regarding the efficacy of certain medications on outcomes in those with A/DUD and ASPD, and has not supported a preferred treatment modality for those with both disorders, thus precluding definitive recommendations for clinicians. No medications are approved for treatment of ASPD; however, medications may be used to treat specific symptoms (e.g., aggression or anger).

Antisocial behavior beginning in childhood has been identified as an independent risk factor in the development of A/DUD; the presence of such childhood behaviors carries a sixfold odds of future development of a substance use disorder. Lee Robins (1966), in her landmark follow-up study of child guidance clinic patients, was one of the first to document this association, which has since been replicated in numerous studies in clinical and general population samples.

CAUSATION

The consistently strong association between ASPD and A/DUD raises questions as to the cause: Does engaging in antisocial behaviors lead to problematic substance use? Or do substance use disorders lead to engagement in aggression and antisocial acts? Research seems to favor the hypothesis that A/DUD is a secondary condition of ASPD. A third possible explanation to account for the association is that there is a shared predisposition or vulnerability underlying both disorders. Several studies using genetically informative samples of both adolescents and adults suggest that alcohol dependence, drug abuse and dependence, and ASPD (as well as childhood antisocial behaviors) share a common genetic vulnerability characterized by a general tendency to externalizing behaviors. This result is consistent with data that suggest A/DUD with ASPD is more heritable than A/DUD alone, as was suggested in the classic Stockholm Adoption Study (1981) indicating that adopted-out sons of fathers with ASPD-like alcoholism had a risk of alcoholism nine times that of adopted-out sons of other fathers.

Evidence from neuropharmacological studies has established some intriguing possibilities. Associations of various behaviors with certain neurotransmitters and their respective enzymes and receptors have been observed, such as serotonin (aggression, impulsivity, low socialization), dopamine (novelty seeking), and monoamine oxidase (depression, aggression, impulsivity). Further, the activity of the autonomic nervous system, which regulates an individual's stress response, appears to be lower in aggressive and antisocial individuals. The interactions among neurotransmitters have led researchers to postulate the existence of multiple neurotransmitter dysfunctions leading to loss of impulse control and an increased appetite for novel experiences.

ASPD is a common concomitant of alcohol and drug use disorders that is associated with accelerated course and poorer outcomes for individuals with these disorders. Although its etiology remained unknown as of 2008, evidence from neuropharmacologic and genetic studies provided some leads. Although symptoms may be managed, as with many personality disorders, there is no proven treatment for ASPD, and findings as of 2008 were equivocal regarding the efficacy of treatment matching using ASPD as an indicator. It is an important disorder to consider in individuals with an A/DUD.

See also **Addictive Personality and Psychological Tests; Childhood Behavior and Later Substance Use; Conduct Disorder and Drug Use; Dopamine; Serotonin.**

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ANXIETY. Anxiety refers to an unpleasant emotional state, a response to anticipated threat or to specific psychiatric disorders. In anxiety, the anticipated threat is often imagined. Anxiety consists of physiological and psychological features. The physiological symptoms can include breathing difficulties (hyperventilation, shortness of breath), palpitations, sweating, light-headedness, diarrhea, trembling, frequent urination, and numbness and tingling sensations. The anxious person is usually hypervigilant and startles easily. The subjective psychological experience of anxiety is characterized by feelings of apprehension or fear of losing control, depersonalization and derealization, and difficulties in concentration. Strains around the performance of social roles (e.g., spouse, parent, wage earner) and certain life situations (e.g., separating from parents when starting school or leaving home, illness) can generate anxiety symptoms. Other factors can contribute to the etiology of anxiety, such as use of alcohol, caffeine and other stimulant drugs (e.g., amphetamine), a family history of anxiety symptoms, or a biological predisposition. In certain cases, recurrent anxiety symptoms will lead an individual to avoid certain situations, places, or things (phobias). In many cases, an anxious emotional state can motivate positive coping behaviors (e.g., anxiety that leads to studying for an exam). When the anxiety becomes excessive and impairs functioning, it can lead to the development of psychiatric illness. Individuals differ in their predisposition to anxiety.

Different constellations of anxious mood, physical symptoms, thoughts, and behaviors, when maladaptive, constitute various anxiety disorders. Panic disorder is characterized by brief, recurrent, anxiety attacks during which individuals fear death

or losing their mind and experience intense physical symptoms. People with obsessive compulsive disorder experience persistent thoughts that they perceive as being senseless and distressing (obsessions) and that they attempt to neutralize by performing repetitive, stereotyped behaviors (compulsions). The essential feature of phobic disorders (e.g., agoraphobia, social phobia, simple phobia) is a persistent fear of one or more situations or objects that leads the individual to either avoid the situations or objects or endure exposure to them with great anxiety. Generalized anxiety disorder is diagnosed in individuals who persistently and excessively worry about several of their life circumstances and experience motor tension and physiologic arousal. Anxiety disorders are the psychiatric illness most frequently found in the general population.

Anxiety states can result from underlying medical conditions, and therefore these conditions should always be looked for when evaluating problematic anxiety. When anxiety develops into a psychiatric illness, various forms of treatment are available to reduce it. The choice of treatment often depends on the specific disorder. Medications may be used, including anxiolytics (e.g., benzodiazepines, buspirone) and antidepressants (e.g., imipramine, fluoxetine). Psychotherapies offered generally consist of cognitive-behavioral interventions (e.g., exposure therapy), but they can include psychotherapy of a supportive nature or more psychodynamically oriented approaches. Some people with severe anxiety may turn to alcohol or nonprescribed sedative-hypnotics for symptom relief, and this in turn may exacerbate the underlying condition.

See also **Prescription Drug Abuse; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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APHRODISIAC. An aphrodisiac is a food, drink, drug, scent, or device that purportedly increases sexual desire or arousal. Even though there is a 5,000-year-old tradition of pursuing sexual enhancement through the use of plants, drugs, and magic, the U.S. Food and Drug Administration (FDA) declared in 1989 that there is no scientific proof that any over-the-counter aphrodisiac works to increase libido and that the only available evidence of aphrodisiacs is, at best, anecdotal and subjective. Double-blind, placebo-controlled studies designed to test the effectiveness of these putative aphrodisiacs are lacking, primarily due to cultural taboos associated with this type of research. Another problem with proving the effectiveness of aphrodisiacs is that many of these substances affect mood but do not have specific sexual effects. Alcohol, for example, has been thought to increase sexual receptiveness. But alcohol is a depressant, and although drinking may decrease inhibitions and thereby lead to increased social contact, it can actually decrease sexual performance.

In the 1990s sildenafil, a phosphodiesterase type 5 (PDE-5) inhibitor, was developed by Pfizer, Inc., to treat angina pectoris (chest pain caused by constriction of coronary arteries). Although Phase I clinical trials yielded disappointing results for the management of angina, scientists discovered that sildenafil could induce marked penile erections. Pfizer therefore decided to market sildenafil for erectile dysfunction, rather than for angina. The drug was patented in 1996 and approved for use in erectile dysfunction by the FDA on March 27, 1998. The first pill approved to treat erectile dysfunction in the United States, it was offered for sale under the brand name Viagra Since the introduction of sildenafil, two other PDE-5 inhibitors have been marketed: vardenafil (Levitra, Bayer AG) and tadalafil (Cialis, Eli Lilly and Company). PDEs participate in the metabolism of the intracellular second messengers, cyclic adenosine monophosphate (cAMP) and cyclic

guanosine monophosphate (cGMP), which are involved in signaling pathways in cavernous smooth muscle. Accumulation of cGMP in the cavernous smooth muscle activates an intracellular cascade that induces a loss of contractile tone of penile blood vessels, thus engorging the tissue with blood and producing an erection. The inhibition of PDE-5 by sildenafil, vardenafil, and tadalafil promotes an erection by inhibiting the degradation of cGMP. Nitric oxide (NO), in turn, increases the production of cGMP to contribute to penile erections. Ultimately, however, even though these compounds make sexual activity possible in men with erectile dysfunction, they do not increase sexual desire, and any potential utility in women has yet to be determined. It is unlikely that PDE-5 inhibitors will have any effect on libido in females either, but these compounds could cause the blood vessels in the vagina (and other genital tissue, including the clitoris) to become engorged with blood, which helps the vagina become properly lubricated in preparation for intercourse. Finally, many botanical medicinal herbs—and drugs derived from these herbs and touted as putative aphrodisiacs—have been shown to have effects on the NO-signaling pathway. For example, the saponins from ginseng (ginsenosides) have been shown to relax the corpus cavernosum, which may aid in the treatment of men suffering from erectile dysfunction. Many plant extracts or purified drugs derived from Chinese medicinal herbs also affect NO pathways.

See also **Ginseng.**

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ARCOS. *See* **Automation of Reports and Consolidated Orders System (ARCOS).**

ARGOT. *See* **Slang Terms in U.S. Drug Cultures.**

ARRESTEE DRUG ABUSE MONITORING (ADAM AND ADAM II).

The Arrestee Drug Abuse Monitoring (ADAM) program was a data collection system that evolved from the landmark Drug Use Forecasting (DUF) program of the National Institute of Justice (NIJ). DUF collected data from 1987 to 1997 in 23 cities across the United States. It was originally designed to collect interview and bioassay (urine) data from persons within 48 hours of arrest. In a brief interview the program collected information on each arrestee's drug use, including drug-use history and arrests. DUF was, however, a convenience sample of arrestees and consequently represented an unknown profile of persons arrested and an unknown segment of arrestees who use drugs.

In 1997 NIJ and Abt Associates redesigned the DUF program to place the data collection effort on a more scientifically defensible basis, renaming it ADAM. The redesign defined each catchment area as a primary city (i.e., Chicago) and its home or surrounding county (Cook County), developed a probability-based sampling plan for each county, sampled booking facilities within each county, and sampled arrestees within each booking facility. ADAM also redesigned the interview instrument to include a number of questions on alcohol use; treatment, health issues, and drug market activity,

and expanded the number of sites. All original sites were reconstituted and retrained on the new protocols from 1998 to 1999. New instrumentation and sampling procedures began in January 2000, marking the beginning of a new trend line for the series.

In its revised form, ADAM had several goals:

- Establish prevalence estimates of numbers of arrestees using drugs in each of the sentinel sites.
- Develop estimates of the number of heavy or chronic drug users in each area.
- Understand the nature and activity of different drug markets over time.
- Understand the characteristics of drug-using offenders (crimes committed, treatment needs, drug careers).
- Understand the relationship between accessing treatment and participating in drug markets in each county annually.
- Work closely with local law enforcement and treatment groups to use ADAM data locally.

The ADAM protocol called for the collection of face-to-face interviews lasting approximately 25 minutes from a probability-based sample of arrestees from sampled booking facilities for 14 consecutive days each quarter. In ADAM the data collection shift is based on the 6- to 8-hour period of a day in each booking facility sampled in which the highest flow of arrestees occurs. The sampling protocol divides each 24-hour period into that heavy period ("flow") and the remaining portion of the 24-hour period when cases have accumulated and interviewers are not present (the "stock" period). Arrestees are sampled proportionately from the stock cases and at timed intervals throughout the flow period, resulting in a representation of the 24-hour period of arrests.

Because individuals are released throughout the day and night before they can be interviewed, each case is weighted to represent its probability of selection. Cases are weighted using the data of all persons arrested during the 14-day window by assigning the probability of being selected using variables that impact such a selection—charge, time of day, day of the week, race or ethnicity, and age. Eligible arrestees are sampled from the total number of persons booked in each facility. All arrestees who have been held no more than 48 hours since arrest are male, and are physically able to respond to questions are eligible to participate. Although data collection for female arrestees continued in many sites after 2000, sampling protocols and case weighting were done only with the male population.

All interviews and specimen provision are voluntary; all interviews and test results are confidential, and no individual-identifying data are collected. Urine specimens are collected at the time of interview, mailed nightly to an external laboratory, and then tested for the presence of each of nine substances. In ADAM a local team collected data at each site directed by a nearby research group working in collaboration with, and trained, funded, and monitored by, a national contractor. Approximately 200 to 250 cases were generated each data collection cycle at each site, although larger, higher-volume sights produced a somewhat greater number of cases

ADAM began as 23 former DUF sites and expanded to a total of 39 sites by 2003. Approximately 20,000 interviews were collected each year. Data continued to show that over half of all arrestees test positive for some illegal substance in their system at the time of arrest, predominantly marijuana. However, like DUF, ADAM provided timely data on the movement of methamphetamine use from its earliest pockets in Southern California to areas such as Des Moines, Iowa; Las Vegas, Nevada; Portland, Oregon; Omaha, Nebraska; and Oklahoma City, Oklahoma, where the number of positive tests increased each year. As was true in its original DUF form, ADAM remained a bellwether for detecting the earliest (and often the heaviest) changes in illegal drug use.

NIJ discontinued ADAM in 2003, citing a lack of funds. Seeing the need for the data ADAM had compiled, the Office of National Drug Control Policy (ONDCP) in 2007 reinstituted collection with Abt Associates in 10 former ADAM sites, renaming the program ADAM II. Ten ADAM II sites were selected, with the focus on sites east of the Mississippi to continue examining any movement of methamphetamine use eastward. The ten sites chosen were New York (Borough of Manhattan), Washington, D.C., Atlanta, Georgia (Fulton

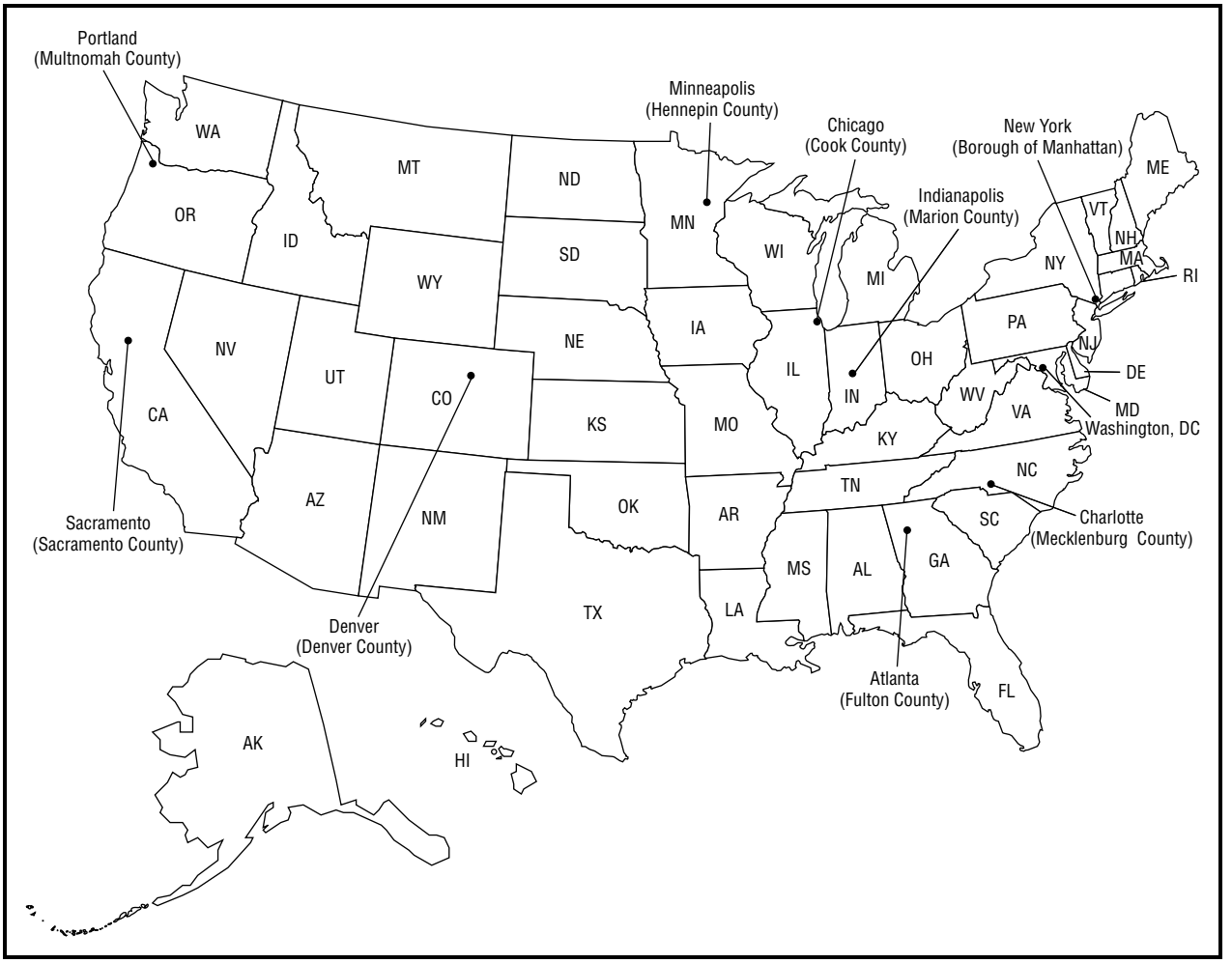

Figure 1. ADAM II sites. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

County), Charlotte, North Carolina (Mecklenburg County), Indianapolis, Indiana (Marion County), Minneapolis, Minnesota (Hennepin County), Chicago (Cook County), Denver, Colorado (Denver County), Portland, Oregon (Multnomah County), and Sacramento, California (Sacramento County).

For ADAM II all protocols, instruments, and sampling remain the same as in ADAM, so trend lines can be developed for each drug at each site. There have been, however, a few important changes from the original ADAM model. Additional questions regarding methamphetamine manufacture were also developed and included in the instruments drug market section and a test for oxycodone was added to the drug test panel. In addition, the national contractor's local field staff now collects data in cooperation with local site directors who maintain working relationships with each booking facility. In ADAM II data are collected in two back-to-back quarters each year (as opposed to each quarter) and annualized to represent the year.

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DANA E. HUNT

ASSESSMENT OF SUBSTANCE ABUSE. *See* **Alcohol, Smoking and Substance Involvement Screening Test (ASSIST); AUDADIS; Drug Abuse Screening Test (DAST); HIV Risk Assessment Battery (RAB); Michigan Alcoholism Screening Test (MAST); Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA); Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA); T-ACE.**

ASSET FORFEITURE. Asset forfeiture is the involuntary relinquishment of money or property without compensation as a consequence of a commission of a crime. Forfeiture laws authorize prosecutors to file civil lawsuits asking a court for permission to take property from a criminal defendant that was either used in the crime or was the fruit of a criminal act. Since the 1970s, federal asset forfeiture laws have been used against drug dealers. By 2000, however, there were many in Congress and the legal community who urged reform of these forfeiture laws, as they have often resulted in harsh and unfair outcomes for innocent third parties. Congress responded by passing the Civil Asset Forfeiture Reform Act of 2000.

FORFEITURE ACT

In 1970, Congress enacted the Comprehensive Drug Abuse Prevention and Control Act, also known as the Forfeiture Act. The Forfeiture Act authorized federal prosecutors to bring civil forfeiture actions against certain properties owned by persons convicted of federal drug crimes. The act was not used much because it limited forfeiture to the property of persons convicted of participating in continuing criminal enterprises. In 1978, Congress amended the law to allow forfeiture of anything of value used or intended to be used by a person to purchase illegal drugs. This amendment expanded the act to allow the forfeiture of all proceeds and property traceable to the purchase of illegal drugs. The amended law authorized the federal government to proceed *in rem* against property. *In rem* forfeiture proceedings are actions taken against the property, not the owner of the property, which allows the government to remove property from persons suspected of a crime without ever charging them with a crime.

Congress amended the Forfeiture Act again in 1984 as part of the Comprehensive Crime Control Act. The amendment authorized the federal government to pursue *in rem* forfeitures of land and buildings. Federal authorities may seize any real property purchased, used, or intended to be used to facilitate narcotics trafficking. Although Congress appears to have intended the law to apply only to drug manufacturing or storage facilities, federal courts have interpreted the law to allow the seizure of any real property, including fraternity houses, hotels, ranches, and private residences. In addition, courts have allowed forfeitures regardless of whether the property was used to store or manufacture drugs.

THE PROCESS OF SEIZING PROPERTY

The process of seizing property under the Forfeiture Act is straightforward. Forfeiture begins with the constructive or actual seizure of property after a warrant has been issued by a federal district court. This warrant must be based on the reasonable belief that the property was used in a crime subject to forfeiture, but this belief can be based on hearsay and circumstantial evidence. After the property is seized, the court holds it until the case is resolved.

In a civil forfeiture proceeding, the government must prove that the property is subject to forfeiture because there is a substantial connection between the property and the crime. If the defendant fails to rebut this proof with sufficient evidence, the government is allowed to keep the property. At the trial, the government's standard of proof is by a preponderance of the evidence, a lesser burden of proof than the criminal standard of a reasonable doubt.

DISTRIBUTION OF PROCEEDS

The Forfeiture Act permits law enforcement agencies to receive a part of the proceeds from property forfeiture. Prior to the 1984 amendments, all revenue derived from a federal asset forfeiture was deposited in the U.S. Treasury general fund. The 1984 law allowed federal law enforcement agencies to keep all proceeds from confiscated property and to use the proceeds to support asset-seizure programs. State and local law enforcement agencies that turned over their seizure cases to federal authorities received up to 80 percent of the profit

after the property had been sold. Many legal scholars criticized this feature of the law, arguing that it detracts from the traditional police function of fighting crime and created incentives for police to pursue forfeitures that lacked probable cause. Proponents of this budgetary scheme argue that drug activity is the source of much violent crime and that the proceeds benefit community programs and increase the capacity to fight violent crime.

Most states also have forfeiture laws upon conviction of certain crimes. These laws often mandate forfeiture of prohibited drugs; property used to contain, protect, or secure prohibited drugs; firearms; and vehicles. In contrast to the federal law, many states require that profits from the sale of forfeited property be deposited in the state's general treasury fund.

DEFENSES TO FORFEITURE

Defendants have employed several defenses to forfeiture, and some have proved successful. If notice and a hearing before a court do not precede the initial seizure, a defendant may argue that forfeiture violates the Due Process Clause of the Fifth and Fourteenth Amendments. If a forfeiture is disproportionate to the offense that gave rise to it, it may be found to violate the Eighth Amendment's Excessive Fines Clause.

Congress has also responded to criticism by enacting the so-called innocent owner defense in civil drug forfeiture cases. These are cases in which forfeiture is sought without prosecution of the owner. A defendant in a civil forfeiture case may invoke this defense if the property was connected with illegal drugs without the owner's knowledge or consent. For example, if the owner of an automobile innocently allows another person to borrow the car and that person commits a drug offense in the car, the owner can offer this defense and retain the car.

As state and federal prosecutors intensified their use of asset forfeiture laws, public dissatisfaction grew. By the early 1990s, the federal government was prosecuting only 20 percent of the individuals from whom it seized property through forfeiture. According to Department of Justice statistics, over 28,000 properties were seized in 1996, with a combined value of $1.264 billion. Critics have argued that the government routinely violates the Fifth Amendment's ban against taking property without due process of law, largely because it sees forfeiture as an easy way to collect funds. Supporters have countered that forfeiture has helped in the war on drugs by stripping criminals of their resources.

CIVIL ASSET FORFEITURE REFORM ACT OF 2000

Congress intervened by passing the Civil Asset Forfeiture Reform Act of 2000, which requires federal prosecutors to show a substantial connection between the property and the crime. In addition, it allows the property to be released by the district court pending final disposition of the case when the owner can demonstrate that possession by the government causes a hardship to the owner. Moreover, the law allows owners of property to sue the government for any damage to the property if the victim of the seizure prevails in a civil forfeiture action.

Though the 2000 act promised more safeguards for an innocent owner's interest in property and placed the burden of proof on the government to establish a preponderance of evidence that the property is subject to forfeiture, the law has not reduced the amount of seized and forfeited property. Although relying solely on the dollar amount of property seized per year to measure the effect of the act is misleading, as the forfeiture of several large assets can raise the yearly amount, the amounts have continued to move upward. In 2006 the Assets Forfeiture Fund/Seized Asset Deposit Fund increased from $659 million in 2005 to $1.25 billion. The 2006 report by the government concluded that there would be a "strong current and future potential stream of assets flowing" into the fund.

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FREDERICK K. GRITTNER

ASSIST. *See* **Alcohol, Smoking and Substance Involvement Screening Test (ASSIST).**

ASSOCIATION FOR MEDICAL EDUCATION AND RESEARCH IN SUBSTANCE ABUSE (AMERSA).

The Association for Medical Education and Research in Substance Abuse (AMERSA) is a national organization of more than 300 medical and allied faculty, which was founded in 1976 for the promotion of education and research in the field of substance abuse. The organization was derived from an informal coalition of U.S. Federal Career Teachers in alcoholism and drug abuse; these career teachers, one on the faculty of each of fifty-five medical schools, were funded by the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) to promote enhanced teaching at their respective medical campuses. The Career Teachers Program, established in 1972, was regarded as a highly successful vehicle for highlighting an issue of considerable importance in the medical curriculum. As the program wound down (it came to an end in 1981), the participants felt it important to secure the continuation of their mission and established AMERSA as a national membership organization open to all medical faculty and faculty in allied health programs.

In the year of its establishment, AMERSA held its first national meeting, which was followed by meetings of increasing attendance in each succeeding year. The national meetings have been the focus of federal participation in teaching programs and have focused on curriculum techniques and new research findings.

AMERSA established a quarterly publication, *Substance Abuse*, in 1979, presenting educational and research findings; it serves as a vehicle for broadening the base of teaching in the members' fields. In addition, a variety of curricula were established by members, with coordination through the AMERSA national headquarters (located in Providence, Rhode Island) and augmented by the Center for Medical Fellowships in Alcoholism and Drug Abuse, located at New York University.

Full membership is available for all persons holding faculty appointments in health-professional schools and/or to those involved in substance abuse education or research. Membership benefits include a free subscription to *Substance Abuse*; reduced rates at the annual conference; and a national voice that supports academic programs in universities, professional schools, and organizations that promote substance abuse education and research.

The organization's members work in a variety of ways to effect their educational ends. Much effort is invested in developing curriculum and curriculum outlines for courses directed at a variety of disciplines and various educational levels. In addition, most members work actively within their respective departments to develop subspecialty expertise—as in psychiatry and internal medicine. Efforts are also directed at schoolwide initiatives—as with programs organized through the deans of medical schools.

See also **Alcohol; Models of Alcoholism and Drug Abuse.**

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MARC GALANTER

ATROPINE. *See* **Scopolamine and Atropine.**

ATTENTION DEFICIT HYPERACTIVITY DISORDER.

The *DSM-IV* taxonomy (American Psychiatric Association 1994) denotes three variants of attention deficit hyperactivity disorder (ADHD): (1) inattentive, (2) hyperactive-impulsive, and (3) attention-hyperactive with impulsivity. The percentage of affected individuals in each ADHD category is respectively estimated at 20 to 30 percent, below 15 percent, and 50 to 70 percent. Females are overrepresented in the inattentive subtype (which has fewer coexisting emotional and behavioral disorders), whereas boys are

more frequently diagnosed with the other two types (which are featured by more severe psychosocial disturbances). The relative absence of behavioral disturbance in the inattentive type may impede treatment initiation (Spencer et al., 2007; Staller & Faraone, 2006). However, symptoms of inattention are more likely to continue into adulthood compared to hyperactive and impulsive symptoms (Hart et al., 1995; Biederman et al., 2000), indicating that this disorder may have the most serious lasting adverse effects on adjustment.

To qualify for diagnosis according to *DSM-IV* criteria, at least six of nine symptoms must be present. Commonly, another diagnosis is also present, particularly conduct disorder or oppositional defiant disorder. Girls with ADHD demonstrate less severe aggression, disruptive behaviors, and hyperactivity as well as a lower prevalence of conduct disorder and oppositional defiant disorder than boys (Staller & Faraone, 2006). Approximately 25 percent of children with ADHD develop antisocial personality disorder (Weiss & Hechtman, 1993; Wender et al., 2001). Mood disorders, anxiety disorders, and substance use disorders are overrepresented in adults who had childhood ADHD (Fayyad et al., 2007).

EPIDEMIOLOGY

A meta-analysis of 102 epidemiological studies concluded that the prevalence of ADHD is 5.29 percent in children and adolescents and 4.4 percent in adults. Boys have 2.45 times greater likelihood of an ADHD diagnosis than girls (Polanczyk & Rohde, 2007). The disorder persists into adulthood in about 30 percent of cases (Polanczyk & Rohde, 2007; Fayyad et al., 2007).

ETIOLOGY

Genetic Factors. Heritability in the range of 0.80 for males and females has been reported in family (Staller & Faraone, 2006) and twin studies (Spencer et al., 2007). Molecular genetic studies strongly implicate the dopaminergic system in the etiology of ADHD (Spencer et al., 2007).

Non-Genetic Factors. Acute brain injury, particularly in the anterior region, frequently results in attentional disturbance and behavioral overactivity. Malnutrition, exposure to alcohol and tobacco additives, and medical illness in the mother during development of the fetus also augment risk for ADHD. Perinatal events, especially hypoxia, also amplify risk for ADHD. There is no compelling evidence as of 2008 indicating that parenting behavior, exposure to food additives, or television cause ADHD.

Neurobiology. Imaging studies have shown morphological abnormalities in the frontal cortex, cerebellum, and subcortical structures; however, the clinical significance of these findings remains uncertain. Functional magnetic resonance imaging (fMRI) studies point to a frontal cortical disturbance that may account for the impairment in executive cognitive capacities along with behavioral undercontrol and poor emotional regulation.

RELATION BETWEEN ADHD AND DRUG ABUSE

Substance use initiation occurs at a younger age and accelerates more rapidly in youths with ADHD (Biederman et al., 1998; Wilens et al., 1998; Molina & Pelham, 2003; Staller & Faraone, 2006). The association between substance use and ADHD is stronger in girls than in boys (Disney et al., 1999; Staller & Faraone, 2006). An association between childhood ADHD and risk for substance use disorder, especially when there is co-occurring childhood conduct disorder (CD), has been documented in many studies (Fayyad et al., 2007). Genetic factors and neurobiological systems are common to both ADHD and the early age onset variant of substance use disorder.

TREATMENT

An 80 percent improvement rate has been reported using psychostimulants in children and adolescents (Markowitz et al., 2003) and 60 percent in adults (Wender et al., 2001). Prognosis following pharmacological treatment is the same for both genders (Pelham et al., 1989). Youths receiving only medication for fourteen months have been reported in one large-scale study to have the same prognosis as youths receiving combined medication management and behavior modification (MTA Cooperative Group, 1999). Disorders co-occurring with ADHD are responsive to behavioral treatments; hence, interventions need to be tailored to the

child's particular pattern of disturbance. Because ADHD in childhood amplifies risk for substance use and substance use disorder, effective treatment may prevent these outcomes.

See also **Amphetamine; Methylphenidate; Pemoline; Psychomotor Stimulant; Risk Factors for Substance Use, Abuse, and Dependence.**

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RALPH TARTER

AUDADIS. The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS) (Grant et al., 1995) is an interview used to assess alcohol and drug use, abuse, and dependence, and many other potentially associated conditions, including medical and psychiatric disorders. The AUDADIS was designed for lay interviewers in large-scale surveys. It is fully structured, meaning that all questions are read to respondents exactly as written.

The AUDADIS was initially developed for the National Longitudinal Alcohol Epidemiologic Survey (NLAES), a survey that was conducted in 1991 and 1992 with 42,862 participants. The AUDADIS was updated into the AUDADIS-IV for the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Grant et al., 2004), conducted with 43,086 participants in 2001 and 2002 (http://niaaa.census.gov/), with a three-year follow up interview to evaluate changes over time. The AUDADIS and AUDADIS-IV were developed by researchers at the Laboratory on Epidemiology and Biometry at the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The

AUDADIS has also been used in a longitudinal general population study of at-risk drinkers (e.g., Hasin et al., 2007).

The AUDADIS-IV was designed to assess alcohol, drug, and psychiatric disorders according to DSM-IV criteria. Alcohol and drug use is covered in detail, substance by substance, as are DSM-IV alcohol and drug abuse and dependence. The psychiatric coverage of the AUDADIS-IV includes mood disorders, including DSM-IV primary major depressive disorder (MDD), bipolar I, bipolar II, and dysthymia. AUDADIS-IV anxiety disorders include DSM-IV primary panic disorder with and without agoraphobia, social and specific phobias, and generalized anxiety disorder. Personality disorders (PDs), assessed on a lifetime basis, included DSM-IV avoidant, borderline, dependent, narcissistic, obsessive-compulsive, paranoid, schizoid, schizotypal, and antisocial personality disorders (APD). Nicotine use and dependence are also covered, but not abuse, as DSM-IV does not include a category for nicotine abuse. All but one of the DSM-IV disorders were assessed by asking about all symptoms and diagnostic criteria for each disorder. Schizophrenia/psychotic disorders were assessed by asking if a doctor had evaluated the participant as having this disorder, since previous studies found that asking the specific symptoms of psychosis in a survey interview took a lot of time in an interview and the results were not reliable or valid. Most DSM-IV disorders are covered in two main time periods: the last 12 months (considered current) and prior to the past 12 months (past). Together, these two periods cover the lifetime history. Personality disorders were asked about on a lifetime basis only, with an explanation to participants that the questions were meant to cover lifelong, stable patterns of thoughts and behaviors.

In addition, in the psychiatric sections, age at onset of each condition was asked, as was number of episodes and duration of longest episode for conditions that could occur more than once. In addition, treatment for all above disorders was covered. Finally, family history of alcohol use disorders, drug use disorders, depression, and antisocial personality disorders were assessed for relatives, including parents, siblings, children, and also more distant relatives.

Medical disorders in the AUDADIS and AUDADIS-IV included those with a hypothesized relationship to alcohol consumption. Disability was assessed for physical and emotional disability. A number of risk factors for and consequences of alcohol use, drug use, and psychiatric disorders were covered, including stigma due to race, gender, religion, weight, disability, and sexual orientation, childhood abuse, neglect and positive family factors, current stresses and social support, and partner violence as perpetrator and victim. Socioeconomic and demographic information is also collected.

The AUDADIS-IV has been used in a computer-assisted format in some studies. In this form, a computer program is designed so that after each question and answer, the computer checks the answer for consistency with some previous answers and presents the next question to the interviewer that needs to be asked. A computer-assisted interview is easier for interviewers when complex branching patterns of questions and answers occur, such as in the AUDADIS. Thus, this type of computerization saves time and reduces errors. DSM-IV diagnoses are produced from the interview data on a group basis by computer program, to be used for research purposes.

The reliability of the AUDADIS and AUDADIS-IV was studied in test-retest reliability studies. In these studies, a series of participants were interviewed once with the interview being tested and then re-interviewed by a second interviewer who did not know the results of the first interview. Reliability for disorders or other conditions was computed by determining the level of agreement of the pairs of interviewers over the level that would be expected by chance (e.g., a coin flip), given how common the disorders are. Examples of test-retest reliability studies of the AUDADIS are those in general population samples (Grant et al. 1995, 2003; Ruan et al. 2008), in a clinical sample of substance abusers (Hasin et al., 1997), and in Puerto Rican primary care patients (Canino et al., 1999). The reliability of alcohol and drug use and dependence is generally excellent. The reliability of the psychiatric sections of the AUDADIS-IV is all in the fair-to-excellent range, similar to or better than the reliability of other interviews that have been used in surveys.

Validity research is more complex than reliability research. Validity studies usually involve testing whether diagnoses obtained from a given assessment procedure agree with other measures or variables in theoretically predicted ways. For an interview such as the AUDADIS, designed for nonclinician interviewers, such testing can include agreement with clinician assessments, with other assessment procedures in widespread use, or other variables such as clinical correlates or longitudinal course. Convergent, discriminative, and construct validities of AUDADIS-IV alcohol use disorder criteria and diagnoses were good to excellent, including when administered to a sample of heavier-than-average drinkers in the United States and in an eleven-country World Health Organization study (Ustün et al. 1997). In addition, clinician reappraisals agreed well with AUDADIS diagnoses of alcohol dependence and major depression in a study conducted in Puerto Rico (Canino et al. 1997).

Controversy exists on whether diagnoses that result from fully structured interviews are the same that experienced, well-trained clinicians would make. The study involving clinical reappraisals in Puerto Rico suggested that the AUDADIS-IV is valid relative to clinician diagnoses, but more studies in different types of samples are needed to ensure that this is a generally applicable result.

See also **Diagnosis of Substance Use Disorders: Diagnostic Criteria; Diagnostic and Statistical Manual (DSM).**

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DEBORAH HASIN

AUDIT. *See* **Alcohol Use Disorders Identification Test (AUDIT).**

AUSTRALIA. Australia is an Anglophone, predominantly European, nation that occupies an island the size of the continental United States. In

1788 the British turned the island into a penal colony, and since then its indigenous population has been supplanted by an English-speaking society of predominantly Anglo-Celtic origin. This population was supplemented by European immigrants after World War II, and a smaller population of Asian immigrants began arriving in the early 1970s. Australia's indigenous people, Aborigines and Torres Strait Islanders, now comprise 2 percent of the population of 20,000,000.

TOBACCO IN AUSTRALIA

Tobacco smoking causes more than 80 percent of all drug-related deaths in Australia, and it was responsible for 8 percent of the burden of disease in 2003, compared to 2 percent from alcohol and 2 percent from illicit drugs. Prior to European settlement, Aboriginal Australians obtained nicotine by chewing the leaves of *Duboisia hopwoodii*, which they call *pituri*, but widespread smoking did not begin in the indigenous population until after the British colonization.

In the early nineteenth century, most of the white male population smoked pipes. This remained the dominant form of tobacco use until the 1900s, when cigarettes gained popularity. Smoking increased among men during and after World War I and among women in the 1950s and 1960s.

Smoking began to decline among Australian men in the 1950s and among women in the 1980s. Daily smoking declined by 40 percent between 1985 (29% of the population) and 2007 (17%), as shown in Figure 1. Australia now has one of the lowest rates of adult smoking in the OECD. Indigenous Australians still have high smoking rates, however: 53 percent of Aboriginal and Torres Strait Islander people were smokers in 2004–2005.

Tobacco Policies. The low contemporary rates of smoking among Australians reflect the effects of the extensive tobacco control measures introduced since the 1970s (see Table 1). The introduction of these policies reflects the success of public health and tobacco control advocates in persuading governments to actively work to reduce smoking prevalence by substantially increasing the price of tobacco, banning its promotion, and reducing opportunities for smoking in the workplace, bars, and public places.

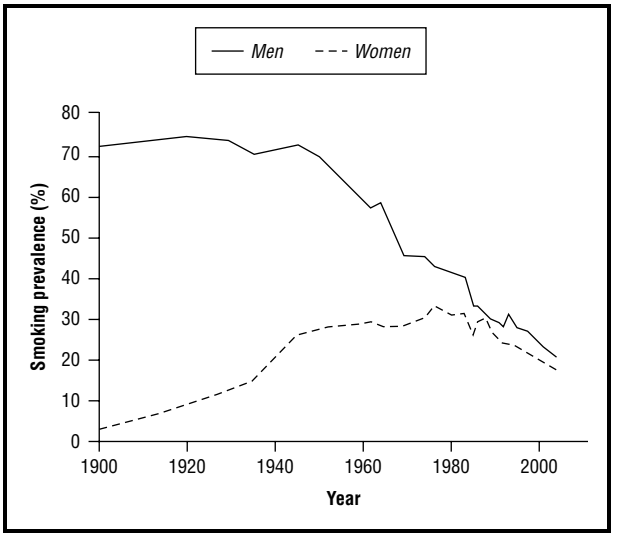

Figure 1. Australian smoking prevalence, 1900–2000. (Sources: Adapted from Tyrrell, 1999 and AIHW, 2007.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Tobacco-related Harm. Tobacco-related harm accounted for an estimated 15,511 deaths in Australia in 2003, while tobacco-related disease was responsible for the loss of 204,788 disability-adjusted life years (DALY). The major causes of both death and disability were lung cancer, chronic obstructive pulmonary disease, and ischemic heart disease. Tobacco-related death and disease has been declining along with the steeply declining prevalence of smoking, although the decline began later in women because of their later uptake of smoking.

ALCOHOL USE

Young working-class males dominated the Australian population from early settlement until the middle of the nineteenth century, leading to a high per capita alcohol consumption during this period. Consumption halved between the Gold Rush in the 1850s and the end of the nineteenth century, as Australia became a settled, urbanized, and family-oriented society, with better education and greater opportunities for recreations other than drinking. Spirits drinking dominated the colonial period but declined with the emergence of a local brewing industry in the late nineteenth century.

A temperance movement in the latter part of the nineteenth century moderated consumption. This movement did not achieve legislated prohibition,

Advertising	• Direct media advertising phased out 1973–1976. • Bans on advertisements that promote smoking 1992. • Advertising at sports events prohibited.
Health warnings	• Mandatory warning labels on cigarette packets 1972. • Graphic health warning on cigarette packs 2006.
Age restrictions Taxation	• Bans on sale of tobacco products to persons under 18. • Federal excise tax on tobacco since 1901. • Taxation on cigarettes changed to a 'per stick' basis 1999. • Excise per stick raised 6 monthly in line with the CPI.
Public smoking Restrictions	• Smoking banned in enclosed public places and workplaces. • 7/8 jurisdictions ban smoking in licensed premises.
Licensing of tobacco retailers	• Licence required to sell tobacco products in 5/8 jurisdictions.
Smoking in cars	• South Australia banned smoking in cars with children under 16 in 2007.
Sales bans	• Sale of smokeless tobacco banned in 1991.

Table 1. Tobacco control measures in Australia. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

but it succeeded in closing hotels at 6:00 p.m. during World War I, a restriction that lasted until the mid-twentieth century, despite the development of a black market in alcohol, colloquially known as "sly-grogging." Alcohol consumption steadily declined from the early 1900s to reach a low in the early 1930s.

Consumption increased between the late 1930s and late 1970s as a result of the nation's growing affluence and the incorporation of alcohol into everyday life in the late 1960s and early 1970s. Alcohol has been heavily promoted via industry sponsorship of sports such as cricket, rugby league football, and horse racing. Wine drinking emerged in the late 1960s, encouraged by European postwar migration, increased travel by Australians to Europe, and the introduction of a sales tax in the early 1970s that favored wine over other forms of alcohol. Alcohol consumption steadily increased during the postwar period, peaking in the late 1970s before declining during the 1980s. It remained relatively steady during the 1990s and 2000s.

In 2003 Australia's per capita alcohol consumption was 7.2 liters per capita, putting it 27th in the world. This was lower than in wine-drinking societies such as France (9.3 liters) and Spain (10.0) and the beer-drinking United Kingdom (9.6), and only marginally higher than New Zealand (6.8), Canada (7.0) and the United States (6.8).

According to the Australian Institute of Health and Welfare (AIHW), in 2006 around 16 percent of Australians abstained from drinking alcohol (20% of women and 13% of men). Of these, 7 percent were ex-drinkers and 9 percent had never consumed a full alcoholic drink. Of the drinkers, 9 percent drank daily, 41 percent drank weekly, and 34 percent drank less than weekly. Women were found to be much more likely to drink less weekly than men were (39% versus 28%). Over half of the drinkers reported that they usually consumed one to two standard drinks (about 10 grams, or 0.6 fluid ounces, of alcohol) per occasion (75% of women and 50% of men). Among men, 59 percent reported either abstaining (13%) or drinking at a low-risk level (46%) and the remainder drank at levels that placed them at risk of short-term (40%) or long-term (10%) harms to their health. Among women, the comparable percentages were: 68 percent abstaining or drinking at low risk; 39 percent at high risk for short-term harms and 10 percent at high risk for long-term harms (AIHW, 2007).

Of the different types of beverages, 47 percent of alcohol is consumed as beer, compared with 32 percent for wine, and 21 percent for spirits. Males are much more likely to consume light and full-strength beer than women, who are much more likely to drink wine. Young men are overrepresented among the substantial minority of drinkers who drink most days of the week and are at risk of short-term harm. The typical quantity consumed and the frequency of drinking among young women has grown closer to that of men, however, reflecting the greater participation of women in paid work, increasing incomes for women, and a weakening of taboos against drinking among women. With the conspicuous exception of Aboriginal alcohol use, ethnic differences in alcohol use have not been investigated.

Alcohol Policy. During the 1970s, state governments liberalized controls on alcohol while increasing treatment for alcohol dependence and introducing random breath testing to reduce alcohol-related motor vehicle crashes. Australia was one of the first countries to introduce compulsory blood testing for persons involved in automobile accidents. It also reduced the blood alcohol level defined as intoxication from 0.08 percent to 0.05 percent. This policy has had strong public support because of its success

in reducing road fatalities. Alcohol was also included as part of the National Campaign Against Drug Abuse, which was launched in 1985, and a National Health Policy on Alcohol was produced in 1989 and updated in 2005.

Alcohol-related Harms. In 2003, alcohol use accounted for an estimated 2 percent of the burden of disease in Australia and averted an estimated 1 percent of disease burden through reduction of cardiovascular disease. It accounted for 1,100 premature deaths and 61,000 DALYs. The major contributors to premature death were alcohol abuse, suicide and self-inflicted injuries, road traffic accidents, and cancers of the oral cavity, esophagus, and the breast (AIHW, 2007).

ILLICIT DRUGS

Cannabis, heroin, amphetamines, cocaine, and MDMA (methylenedioxymethamphetamine, or "Ecstasy") have been the major illicit drugs used in Australia (see Figure 2). Cannabis is illegally grown and amphetamines are produced in the country, while opiates and cocaine are imported. The 2004 National Drug Strategy Household Survey found that cannabis was used by 34 percent of persons over the age of 14 years at some time in their lives, while 11 percent reported having used it in the past year. Lifetime cannabis use increased between 1973 and 1998 but has declined since (AIHW, 2007).

At the same time, around 2 percent of persons over 14 had injected heroin at least once, and just under 0.5 percent reported that they had used heroin in the past year. There were estimated to be 74,000 dependent heroin users in 1997–1998. Heroin use increased during the middle 1990s, but it declined steeply after the onset of a heroin shortage at the beginning of 2001. Amphetamine derivates had been used by 9 percent of Australian adults, and 11 percent of those 20 to 29 years of age reported using these substances in the previous year. Males are more likely than females to have used amphetamines, and they typically do so in their late teens. The use of the amphetamine analogue MDMA increased from 2 percent in 1995 to 8 percent in 2004, with 3 percent reporting use in the previous year. Lifetime use of cocaine is 5 percent of adults, with 1 percent using in the previous year.

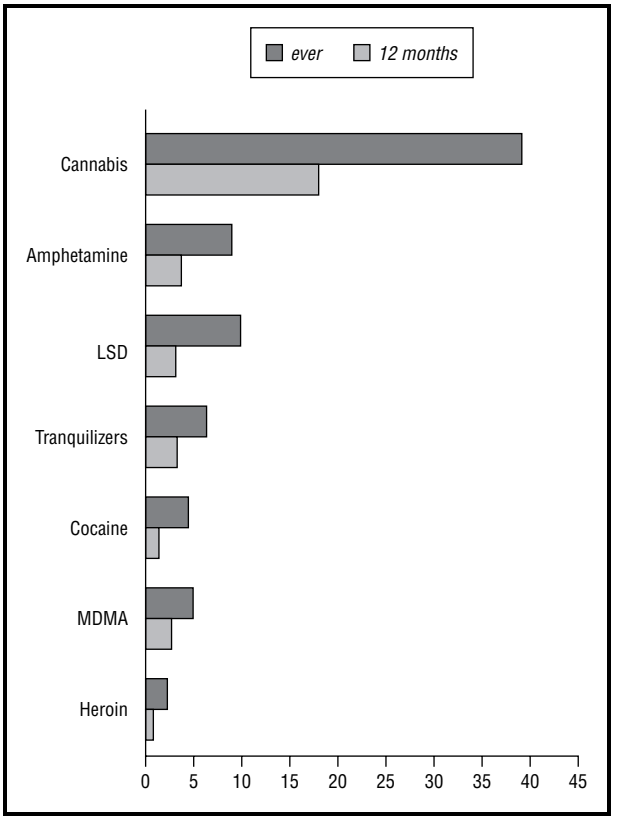

Figure 2. Prevalence of illicit drug use among Australian adults in 2004. (Adapted from AIHW, 2007.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Australia has a higher rate of lifetime cannabis use (34%) than the United States (33%), the United Kingdom (22%) and the Netherlands (18%). The prevalence of heroin dependence in Australia is similar to that in the European Union and the United Kingdom, and it is a little higher than in the United States, which has a much higher rate of cocaine use (10%) than Australia (3%).

Illicit-drug Policy. The aim of the 1986 National Campaign Against Drug Abuse was to "minimize the harmful effects of drugs on Australian society" by increasing public education and expanding treatment for opioid and other drug dependence. Australia's harm-minimization approach was exemplified by its response to the HIV epidemic in the early 1980s. This effort involved frank public education campaigns, the introduction of needle and syringe exchange programs, the diversion of drug offenders into treatment, the expansion of methadone maintenance and drug-free treatment programs, and not

enforcing laws against the possession of injecting equipment.

Bipartisan support for harm-minimization weakened in 1997 when the Prime Minister, John Howard, and the cabinet vetoed a proposed trial of prescribing heroin for opioid dependent persons, a program that had been approved by a majority of state and federal health and law enforcement ministers. The federal government subsequently allocated more than $A500 million to education, treatment, and law enforcement to reduce opioid overdose deaths and illicit-drug-related crime. The prime minister also directly funded abstinence-oriented NGO (nongovernmental organization) treatment services, and he created the Australian National Council on Drugs, whose chair, Brian Watters, opposed harm minimization.

Harm minimization was retained in 1998 in a compromise national policy but broadened to include "abstinence-oriented strategies." Until the election of a Labor government in December 2007 national drug policy used the rhetoric of being "tough on drugs" to cover a strong budgetary emphasis on law enforcement and interdiction, together with increased funding for abstinence-oriented and methadone treatment and programs that divert drug users into treatment.

Illicit Drug-Related Harm. Illicit drug use in Australia accounts for around 2 percent of the burden of disease. This is primarily attributable to heroin overdose deaths and deaths and illness from Hepatitis C infections. The number of fatal overdoses rose from 6 in 1964 to over 1,000 in 1999, before declining by 40 percent in 2001. Australia has low rates of HIV infection among injecting drug users (IDUs), with fewer than 8 percent of new cases being IDUs and 3 percent of IDUs infected with HIV. This low rate of infection reflects Australia's geographic isolation, the low numbers of visitors and immigrants, and the early introduction of needle and syringe exchange programs. Among IDUs, 50 percent are infected with Hepatitis C, and the rate of new Hepatitis C infections is estimated to be 15 percent per year.

See also **Alcohol; Amphetamine; Amphetamine Epidemics, International; Cannabis, International Overview; Foreign Policy and Drugs, United States; Harm Reduction; Hepatitis C Infection; Heroin; International Drug Supply Systems; Tobacco.**

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WAYNE HALL
CORAL GARTNER

AUTOMATION OF REPORTS AND CONSOLIDATED ORDERS SYSTEM (ARCOS).

The Controlled Substances Act of 1970 requires all manufacturers and distributors of controlled substances to report their activities to the attorney general of the United States, via the Drug Enforcement Administration (DEA), on a regular basis (quarterly or monthly). The DEA uses the Automation of Reports and Consolidated Orders System (ARCOS) to collect and track this information, and it reports on a statistically valid sampling of all information received.

CLASSIFICATION OF CONTROLLED SUBSTANCES

The substances covered by the Controlled Substances Act include legal prescription and over-the-counter pharmaceuticals as well as potentially addictive or abusable illegal drugs. The U.S. government classifies drugs into five schedules (categories), based on potential for abuse and addiction, potential harmfulness, and medical utility.

The drugs classified into Schedule I have no accepted medical utility in the United States but have tremendous potential for abuse and addiction. Some Schedule I drugs are methamphetamine, MDMA (street name: Ecstasy), PCP, heroin, LSD, marijuana, and crack. Schedule II drugs have

high potential for abuse, dependence, or addiction but may have accepted medical uses in the United States. Drugs in this category are many of the prescription stimulants, depressants, and narcotics. Some Schedule II drugs are codeine, morphine, cocaine, and Ritalin. Prescribers of Schedule II drugs must use special forms and cannot indicate refills. These prescriptions must be hand-delivered to the pharmacy, except under specific emergency circumstances. Drugs in Schedules III, IV, and V are progressively less addictive or prone to abuse or dependence. These drugs may be similar to those in Schedule II but with lower narcotic concentrations. Some Schedule III drugs are sedatives, "crank," anabolic steroids and other body-building drugs, Tylenol with codeine, and some milder sedatives and barbiturates. Schedule IV contains many of the milder antianxiety, antidepressant, appetite suppressant, stimulant, and sleep-inducing drugs, such as Valium, Librium, Ativan, Meridia, Ambien, Halcion, and Cylert, as well as Rohypnol. Schedule V drugs pose the lowest risk of abuse and dependence; they include nonprescription substances such as commercial cough medicines and antidiarrheals.

ARCOS PROGRAM DESCRIPTION

The DEA requires registration and regulatory compliance by all manufacturers of controlled substances; all health care providers licensed or certified to prescribe, dispense, or administer them; and all pharmacies permitted to fill prescriptions. The DEA is also tasked with monitoring the flow of controlled substances across national borders.

ARCOS functions as a comprehensive tracking system for controlled substances, extending from the point of manufacture to distribution for retail use in dispensing facilities such as hospitals, medical offices, clinics, other in- or outpatient settings, and commercial sales through pharmacies or other registered retailers, such as chain stores with pharmacy departments. Manufacturers, distributors, and retailers must track and report all Schedule II through Schedule V activities on a regular basis. ARCOS synthesizes the data from approximately 1,100 data sources into a report form submitted to the DEA. By comparing manufacture and distribution reports, the government regulating agencies are better able to determine the means by which drugs are moved from legal to illegal venues, which is called *drug diversion*. Among the most common ways in which controlled substances are illegally diverted are by physicians (most frequent) or other health care practitioners who prescribe medication for abusing/dependent individuals or who write prescriptions to known drug dealers; pharmacists who falsify records (second most frequent) and then sell their controlled substance inventory illegally; staff at dispensing facilities who steal and then traffic drugs; commercial theft (such as burglary); and forgery of prescriptions, either by theft of prescription pads or by changing quantity, dose, or refill amounts on legitimately written prescriptions.

The DEA has an Office of Diversion Control (ODC) designed to investigate, track, and trend drug-diversion activities. The office is multidisciplinary and uses the expertise of chemists, pharmacologists, information technology experts, field operations investigators, and special agents. The ODC's work is simplified as a result of the data collected and reported by ARCOS.

Since 2005, ARCOS has employed an electronic data interchange (EDI) reporting system, which has dramatically increased the efficiency of the former paper-based reporting mechanism. DEA registrants using this system log onto the ODC Web site's secured portal and upload their required reports instantly.

Only pharmaceutical manufacturers and distributors report to ARCOS. Manufacturers of controlled substances are required to report their inventories, acquisitions and dispositions of all substances contained in Schedule I as well as narcotic and gamma-hydroxybutyric acid (GHB) substances in Schedule III. They must also report all synthesizing activities involving Schedules I and II, narcotics, and GHB as well as some specific controlled psychotropic drugs contained in Schedules III and IV. Distributors of controlled substances are mandated to report their inventories, acquisitions, and dispositions of all substances contained in Schedules I and II as well as narcotic and gamma-hydroxybutyric acid (GHB) substances in Schedule III. As of 2008, approximately 1,100 manufacturers and distributors report to ARCOS; this is a very small number in comparison to the more than one million registrants contained in the Drug Enforcement Administration's (DEA) Controlled Substances Act database.

For each annual data-reporting period, myriad reports are generated, depending on the needs and requirements of the DEA as well as the reporting states and other entities. The summary data is synthesized into six major reports:

- *Retail Drug Distribution by Zip Code for Each State* reports drug amounts, in grams, distributed to each retail registrant, sorted by state and zip code.
- *Retail Drug Distribution by Drug Code for Total U.S.* is a quarterly tally of the total drug quantities distributed to each registrant, sorted by state.
- *Quarterly Distribution in Grams per 100K Population* indicates quarterly drug consumption, sorted by state, by number of grams per 100,000 population.
- *Cumulative Distribution in Grams per 100K Population* is similar to the report above, with a cumulative yearly tally. Every state is ranked in ascending order by each drug.
- *Statistical Summary for Retail Drug Purchases* sorts average purchase for each drug by business activity and state.
- *U. S. Summary of Retail Drug Purchases* presents a cumulative picture of the average purchase of each drug, by business activity, for the entire United States.

See also **Controlled Substances Act of 1970; Controls: Scheduled Drugs/Drug Schedules, U.S.**

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PAMELA V. MICHAELS

AYAHUASCA. The use of naturally psychoactive products is a feature of shamanic practices across the globe, but the peoples of the Americas seem to have been blessed with an extraordinary variety. Archeological evidence of the use of psychoactive preparations in the Americas dates back thousands of years, and the same archeological record shows the high importance placed on these substances in the religious and cultural life of the Americas prior to European contact. Upon the conquest of the Americas, the use of these preparations was suppressed by the Christian Church, which rightly saw the use of these drugs as a threat to its religious hegemony over the peoples of the New World. In spite of this, and in spite of continued threats of suppression as a part of various national and international drug prohibition regimes, the use of psychoactive drugs in the spiritual life of native and mestizo peoples in the Americas has continued to the early twenty-first century. In recent decades the acceptance of these drugs in cultural settings outside of their traditional homes has slowly seeped into more Westernized elements of society in both Europe and the Americas. Among the most notable of these psychoactive plant-based churches are those that center their ritual existences around the hallucinogenic preparation ayahuasca. Two churches, the Santo Daime and Uniao do Vegetal (UDV), which had their origins among the mestizo populations of the Brazilian interior in the mid-twentieth century, have spread the ritual use of ayahuasca from Amazonia first, then via the influx of people from the Amazon backcountry, to the great cities of Brazil. From the cities of Brazil, these churches have spread in recent years to the cosmopolitan cities of the developed world.

Moving from the other cultural direction have been both scientists and "ayahuasca tourists." Among the early members of the latter class are the Beat writers Allen Ginsberg and William S. Burroughs, whose *The Yage Letters* remains a common entry point for curious Westerners to the literature and experience of ayahuasca. Combining the roles of scientist, shaman, and tourist/adventurer is perhaps the most important figure in the cross-cultural journey of ayahuasca in recent years, Terrence McKenna, who with his brother Dennis has perhaps done more than any other individual to promulgate the study and use of natural hallucinogens, or to use his own term, *entheogens*, outside of

their traditional context in the Amazon and elsewhere. Terrence, who died in 2000, was the adventurer and shaman of the pair, writing numerous books such as *The Invisible Landscape* and *The Archaic Revival*. Both chronicle his experiences with traditional and pharmacological psychedelic drugs and his hypothesis that psychedelic drug use was a source of both religious belief and the evolution of human intelligence. Dennis was the scientist of the pair, and he produced a number of contributions to our understanding of the pharmacology of psychoactive ethnobotanical preparations such as ayahuasca.

Ayahuasca is an Amazonian herbal preparation that has most likely been used for religious and shamanic purposes in the Amazon basin for thousands of years, although the first definitive reports of its use by outside explorers may be traced to the mid-nineteenth century. Ayahuasca, which is variously known as *Caapi*, *Natema*, *Mihi*, *Yage*, *La Purga*, or *Santo Daime* depending on the cultural context in which it is encountered, is a Quechua word meaning "spirit vine," which roughly encapsulates its traditional purpose and use in the cultures of the Amazon and their more recent global offshoots. Ayahuasca is a brew of various plants, usually slow-boiled to concentrate the plant extracts, which is drunk by the user to obtain its effects. It is prepared in a variety of ways comparable to the large number of cultures in which it is important, but it always contains the vine *Banisteriopsis caapi* and typically a plant containing dimethyltryptamine (DMT), most often *Psychotria viridis*. Usually consumed under the guidance of a shaman, who often uses chants and a low-light environment to guide the experience, the combination produces several hours of profound hallucinatory experiences that, in the context of the compound's use, allow contact with the spirit world and permit spiritual physical and psychological healing to occur. The content of the hallucinations often contains consistent elements across users, with visions of serpents and spiritual beings of various sorts being quite common. Visions of death can also occur with some frequency, as can reactions of intense fear in some users, properties—in addition to the nausea it produces—that make ayahuasca unlikely to be used at all outside of a ritual or therapeutic setting.

The compound nature of ayahuasca makes it one of the most advanced and potent products of any traditional pharmacopoeia in the world. To understand the pharmacological sophistication of the prehistoric shamans who created ayahuasca, it is necessary to understand the psychoactive constituents of the two plants from which it is made. *Banisteriopsis caapi* contains significant amounts of the β-carbolines harmaline and harmine, both of which are potent inhibitors of the enzyme monoamine oxidase (MAO), as well as the source of a number of other significant effects on the nervous system. *Psychotria viridis* is rich in the powerful hallucinogen DMT. DMT, however, is broken down rapidly in the gut and blood by MAO, rendering it inactive when ingested alone. However, when extracts of the two plants are combined, the MAO inhibition provided by the alkaloids in *Banisteriopsis caapi* permits DMT to enter first the bloodstream and then the brain where it exerts its effects on consciousness and perception. Interestingly, both DMT and β-carbolines are present endogenously in the human body. DMT has been implicated in the production of dreams and β-carbolines in anxiety and depression. As mentioned above, a number of preparations of ayahuasca exist: Some contain other psychoactive plants such as tobacco or cocoa leaves, and others like *pharmahuasca* are merely purified DMT and harmine in pill form, seen sometimes in the developed world.

With regard to human psychological health, the few studies of the psychological traits of those who use ayahuasca in a ritual setting on a regular basis have shown reduced levels of panic and hopelessness, and a generally improved outlook. Physically, besides the acute nausea the drug often produces, there is little evidence of negative effects. What research has been done on ayahuasca and its major constituents, DMT and the harmala alkaloids, suggests that its beneficial effects on the psyche are dependent on the set and setting of an individual's encounter with the drug. Whereas those who use ayahuasca in its traditional cultural milieu may often gain from the experience, those who approach it as tourists or thrill seekers are more likely to have neutral or negative psychological outcomes in the absence of an experienced shaman to guide the *journey*, as the ayahuasca

experience is often called. In traditional contexts and in the newer ayahuasca-using churches, ayahuasca seems to actually be beneficial in reducing the abuse of other substances. For these reasons, ayahuasca seems unlikely to become an abused drug (indeed, no reliable reports of ayahuasca abuse are available), although its use might become more common as the culture of the developed world becomes more accustomed to the ancient spiritual technology ayahuasca represents in its traditional Amazonian context.

See also **Hallucinogenic Plants; Hallucinogens; Plants, Drugs From.**

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B

BARBITURATES. Barbiturates refer to a class of general central nervous system depressants that are derived from barbituric acid, a chemical discovered in 1863 by the Nobel Prize winner in chemistry (1905) Adolf von Baeyer (1835–1917). Barbituric acid itself is devoid of central depressant activity; however, German scientists Emil Hermann Fischer and Joseph von Mering made some modifications to its structure and synthesized barbital, which was found to possess depressant properties. Scientists had been looking for a drug to treat anxiety and nervousness but without the dependence-producing effects of opiate drugs such as opium, codeine, and morphine. Other drugs such as bromide salts, chloral hydrate, and paraldehyde were useful sedatives, but they all had problems such as toxicity or they left such a bad taste in patients' mouths that they preferred not to take them. Fischer and von Mering noted that barbital produced sleep in both humans and animals. It was introduced into chemical medicine in 1903 and was soon in widespread use.

By 1913, the second barbiturate, phenobarbital, was introduced into medical practice. Since that time, more than 2,000 similar chemicals have been synthesized but only about 50 of these have been marketed. Although the barbiturates were quickly used to treat a number of disorders effectively, their side effects were becoming apparent. The chief problem, an overdose, can result in respiratory depression, which can be fatal. By the mid-1950s, more than 70 percent of admissions to a poison-control center in Copenhagen, Denmark, involved barbiturates. Additionally, it became apparent that the barbiturates were subject to abuse, which could lead to dependence, and that a serious withdrawal syndrome could ensue when the drugs were abruptly discontinued. In the 1960s, the introduction of a safer class of hypnotic drugs, the benzodiazepines reduced the need for barbiturates.

Barbiturates are dispensed in distinctly colored capsules making them very easy to identify by the lay public. In fact, users within the drug culture often refer to the various barbiturates by names associated with their physical appearance. Examples of these names include blue birds, blue clouds, yellow jackets, red devils, sleepers, pink ladies, and Christmas trees. The term *goofball* is often used to describe barbiturates in general. All barbiturates are chemically similar to barbital, the structure of which is shown in Figure 1.

All barbiturates are general central nervous system depressants. This means that sedation, sleep, and even anesthesia will develop as the dose is increased. Some barbiturates also are useful in reducing seizure activity and so have been used to treat some forms of epilepsy. The various barbiturates differ primarily in their onset and duration of action, ability to enter the brain, and the rate at which they are metabolized. These differences are achieved principally by adding or subtracting atoms to the two branches on position #5 in Figure 1. The barbiturates are classified on the basis of their duration of action, which ranges from ultrashort-acting to long-acting. The onset of action of the ultrashort-acting barbiturates occurs in seconds

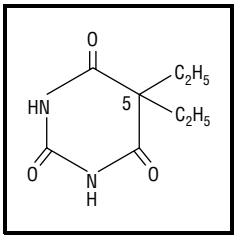

Figure 1. Chemical structure of barbital. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

and lasts a few minutes. The short-acting compounds take effect within a few minutes and can last four to eight hours, while the intermediate- and long-acting barbiturates can take almost an hour to take effect but last six to twelve hours. Table 1 lists the common barbiturates, their trade names, typical route of administration, and plasma half-life. The plasma half-life is a measure of how long the drug remains in the blood, but not how long the effects last, although it does provide a general indication of when to expect the effects to wane (a half-life of five hours means that one-half of the drug will be removed from the system in five hours; one-half of the remaining drug will be removed during the next five hours, etc.).

Drug class and generic names	Trade names	Routes of administration*	Half-life (in hours)
Ultrashort-acting:			
methohexital sodium	Brevital	IV	3.5–6**
thiamylal sodium	Surital	IV	†
thiopental sodium	Pentothal	IV	3–8**
Short-acting:			
butalbital	‡	PO	35
hexobarbital	Sombulex	PO; IV	3–7
pentobarbital	Nembutal	PO; IM	15–48
secobarbital	Seconal	PO; IM	15–40
Intermediate-acting:			
amobarbital	Amytal	PO; IM	8–42
aprobarbital	Alurate	PO	14–34
butabarbital	Butisol	PO	34–42
talbutal	Lotusate	PO	†
Long-acting:			
phenobarbital	Luminal	PO; IV	24–96
mephobarbital	Mebaral	PO	11–67

*IV = intravenous; IM = intramuscular; PO = oral.
**Values are for whole body, half-life in the brain is less than 30 minutes.
†Half-life data not available for human subjects.
‡Various preparations in combination with acetaminophen.

Table 1. Classification of barbiturates on the basis of duration of action. (Source: Rall, 1990, Csáky, 1979.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

EFFECTS ON THE BODY AND THERAPEUTIC USES

Barbiturates affect all excitable tissues in the body. However, neurons are more sensitive to their effects than other tissues. The depth of central nervous system depression ranges from mild sedation to coma and depends on many factors including which drug is used, its dose, the route of administration, and the level of excitability present just before the barbiturate was taken. The most common uses for the barbiturates are still to promote sleep and to induce anesthesia. Barbiturate-induced sleep resembles normal sleep in many ways, but there are a few important differences. Barbiturates reduce the amount of time spent in rapid eye movement or REM sleep—a very important phase of sleep. Prolonged use of barbiturates causes restlessness during the late stages of sleep. Since the barbiturates remain in our bodies for some time after we awaken, there can be residual drowsiness that can impair judgment and distort moods for some time after the obvious sedative effects have disappeared. Curiously, some people are actually excited by barbiturates, and the individual may even appear inebriated. This paradoxical reaction often occurs in the elderly and is more common after taking phenobarbital.

The general use of barbiturates as hypnotics (sleeping pills) has decreased significantly, since they have been replaced by the safer benzodiazepines. Phenobarbital and butabarbital are still available, however, as sedatives in a number of combination medications used to treat a variety of inflammatory disorders. These two drugs also are used occasionally to antagonize the unwanted overstimulation produced by ephedrine, amphetamine, and theophylline.

Since epilepsy is a condition of abnormally increased neuronal excitation, any of the barbiturates can be used to treat convulsions when given in anesthetic doses; however, phenobarbital has a selective anticonvulsant effect that makes it particularly useful in treating grand mal seizures. This selective effect is shared with mephobarbital and metharbital. Thus, phenobarbital is often used in hospital emergency rooms to treat convulsions such as those that develop during tetanus, eclampsia, status epilepticus, cerebral hemorrhage, and poisoning by convulsant drugs.

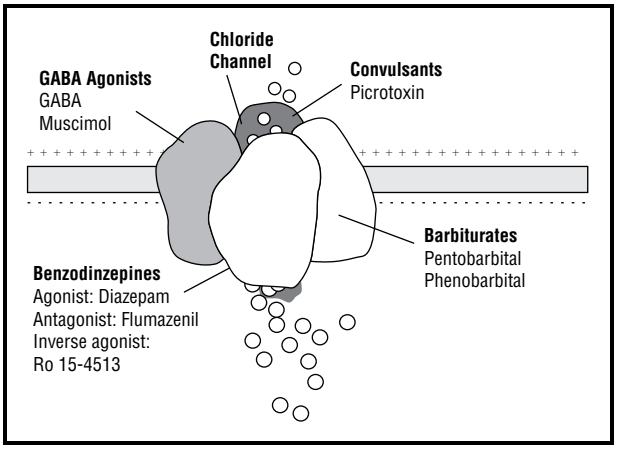

Figure 2. Barbiturates. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The benzodiazepines are, however, gradually replacing the barbiturates in this setting as well.

It is not completely understood how barbiturates work but, in general, they act to enhance the activity of GABA on GABA-sensitive neurons by acting at the same receptor on which GABA exerts its effects (see Figure 2). GABA is a neurotransmitter that normally acts to reduce the electrical activity of the brain; its action is like a brake. Thus, barbiturates enhance the braking effects of GABA to promote sedation. There is an area in the brain called the reticular activating system, which is responsible for maintaining wakefulness. Since this area has many interconnecting or polysynaptic neurons, it is the first to succumb to the barbiturates, and that is why an individual becomes tired and falls asleep after taking a barbiturate.

PHARMACOKINETICS AND DISTRIBUTION

The ultrashort-acting barbiturates differ from the other members of this class mainly by the means by which they are inactivated. Methohexital and its relatives are very soluble in lipids (i.e., fatty tissue). The brain is composed of a great deal of lipid; when the ultrashort-acting barbiturates are given intravenously, they proceed directly to the brain to produce anesthesia and unconsciousness. After only a few minutes, however, these drugs are redistributed to the fats in the rest of the body so their concentration is reduced in the brain. Thus, recovery from IV barbiturate anesthesia can be very fast. For this reason, drugs such as methohexital and thiopental are used primarily as intravenous anesthetic agents and not as sedatives.

The other longer-acting barbiturates must be metabolized by the liver into inactive compounds before the effects wane. Since these metabolites are more soluble in water, they are excreted through the kidneys and into the urine. As is the case with most drugs, metabolism and excretion is much quicker in young adults than in the elderly and infants. Plasma half-lives are also increased in pregnant women because the blood volume is expanded due to the development of the placenta and fetus.

TOLERANCE, DEPENDENCE, AND ABUSE

Repeated administration of any number of drugs results in eventual compensatory changes in the body. These changes are usually in the opposite direction of those initially produced by the drug such that more and more drug is needed to achieve the initial desired effect. This process is called tolerance. There are two basic mechanisms for tolerance development: tissue tolerance and metabolic or pharmacokinetic tolerance. Tissue tolerance refers to the changes that occur on the tissue or cell that is affected by the drug. Metabolic tolerance refers to the increase in the processes that metabolize or break down the drug. This process generally occurs in the liver. Barbiturates are subject to both types of tolerance development.

Tolerance does not develop equally in all effects produced by barbiturates. Barbiturate-induced respiratory depression is one example. Barbiturates reduce the drive to breathe and the processes necessary for maintaining a normal breathing rhythm. Thus, while tolerance is quickly developing to the desired sedative effects, the toxic doses change to a lesser extent. As a result, when the dose is increased to achieve the desired effects (e.g., sleep), the margin of safety actually decreases as the dose comes closer to producing toxicity. A complete cessation of breathing is often the cause of death in barbiturate poisoning (Rall, 1990).

If tolerance develops and the amount of drug taken continues to increase, then physical dependence can develop. This means that if the drug is suddenly stopped, the tissues' compensatory effects become unbalanced and withdrawal signs appear. In the case of barbiturates, mild signs of withdrawal include apprehension, insomnia, excitability, mild tremors, and loss of appetite. If the dose was very high, more severe signs of withdrawal can occur,

such as weakness, vomiting, decrease in blood pressure regulatory mechanisms (so that pressure drops when a person rises from a lying position, called orthostatic hypotension), increased pulse and respiratory rates, and grand mal (epileptic) seizures or convulsions. Delirium with fever, disorientation, and hallucinations may also occur. Unlike withdrawal from the opioids, withdrawal from central nervous system depressants such as barbiturates can be life threatening. The proper treatment of a barbiturate-dependent individual always includes a slow reduction in the dose to avoid the dangers of rapid detoxification.

Few, if any, illegal laboratories manufacture barbiturates. Diversion of licit production from pharmaceutical companies is the primary source for the illicit market. Almost all barbiturate users take it by mouth. Some try to dissolve the capsules and inject the liquid under their skin (called skin-popping) but the toxic effects of the alcohols used to dissolve the drug and the strong alkaline nature of the solutions can cause lesions of the skin. Intravenous administration is a rare practice among barbiturate abusers.

Many barbiturate users become dependent to some degree during the course of treatment for insomnia. This type of problem is called iatrogenic, because it is initiated by a physician. In some instances the problem will be limited to continued use at gradually increasing doses at night, to prevent insomnia that is in turn due to withdrawal. However, some individuals who are susceptible to the euphoric effects of barbiturates may develop a pattern of taking increasingly larger doses to become intoxicated, rather than for the intended therapeutic effects (for example, to promote sleepiness). To achieve these aims, the person may obtain prescriptions from a number of physicians and take them to a number of pharmacists—or secure their needs from illicit distributors (dealers). If the supply is sufficient, the barbiturate abuser can rapidly increase the dose within a matter of weeks. The upper daily limit is about 1,500 to 3,000 milligrams; however, many can titrate their daily dose to the 800 to 1,000 milligram range such that the degree of impairment is not obvious to others. The pattern of abuse resembles that of ethyl (drinking) alcohol, in that it can be daily or during binges that last from a day to many weeks at a time. This pattern of using barbiturates for intoxification is more typically seen in those who, from the beginning, obtain barbiturates from illicit sources rather than those who began by seeking help for insomnia.

Barbiturates are sometimes used along with other drugs. Often, the barbiturate is used to potentiate, or boost, the effects of another drug upon which a person is physically dependent. Alcohol and heroin are commonly taken together in this way. Since barbiturates are "downers," they also are used to counteract the unwanted overstimulation associated with stimulant-induced intoxication. It is not uncommon for stimulant abusers (on cocaine or amphetamines) to use barbiturates to combat the continued "high" and the associated motor disturbances associated with heavy and continued cocaine use. Also, barbiturates are used to ward off the early signs of withdrawal from alcohol.

Treatment for barbiturate dependence is often conducted under carefully controlled conditions, because of the potential for severe developments, such as seizures. Under all conditions, a program of supervised withdrawal is needed. Many years ago, pentobarbital was used for this purpose and the dose was gradually decreased until no drug was given. More recently, phenobarbital or the benzodiazepines—chlordiazepoxide and diazepam—have been used for their greater margin of safety. The reason that the benzodiazepines sometimes work is because the general central nervous system depressants—barbiturates, alcohol, and benzodiazepines—develop cross-dependence to one another. Thus a patient's barbiturate or alcohol withdrawal signs are reduced or even eliminated by diazepam.

See also **Withdrawal.**

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BARBITURATES: COMPLICATIONS.

Barbiturates are central nervous system (CNS) depressants (downers). These drugs produce sedative, hypnotic, and anesthetic effects. Depending on the dose used, any single drug in this class may produce sedation (decreased responsiveness), hypnosis (sleep), and anesthesia (loss of sensation). A small dose will produce sedation and relieve anxiety and tension; a somewhat larger dose taken in a quiet setting will usually produce sleep; an even larger dose will produce unconsciousness. The sleep produced by barbiturates, however, is not identical with normal sleep. Normal sleep consists of several phases, including slow-wave sleep, or deep sleep, and rapid-eye-movement (REM) sleep. In the REM sleep phase, skeletal muscles relax, eyes move rapidly and frequently, and dreaming occurs. Dreaming is believed to play an important role in learning and memory. Barbiturates decrease REM (or dreaming) sleep, which may explain why the sleep associated with barbiturates is less restorative than natural sleep.

As is true for most drugs that act on the CNS, the effects of these drugs are also influenced markedly by the user's previous drug experience, the circumstances in which the drug is taken, and the route of administration of the drug. For example, a dose taken at bedtime may produce sleep, whereas the same dose taken during the daytime may produce a feeling of euphoria, incoordination, and emotional response. This, in many ways, is what happens with alcohol intoxication. In fact, the behavioral effects of this class of drugs is very similar to those observed after drinking alcohol, and the user may experience impairment of skills and judgment not unlike that experienced with alcohol. It is therefore not surprising that the effects of barbiturates are enhanced when taken in combination with alcohol, anti-anxiety drugs (benzodiazepines), and other CNS depressants such as opioids, antihistamines, and over-the-counter cough and cold medications containing these drugs. Barbiturates, however, differ from some other sedative-hypnotic drugs in that they do not elevate the pain threshold. In fact, patients experiencing severe pain may become agitated and delirious if they are given barbiturates without also receiving analgesics (pain killers).

Barbiturates are generally classified as being long, intermediate, short, and ultra-short acting on the basis of their duration of effect. The long-acting barbiturates, such as phenobarbital, which were at one time mainly employed as daytime sedatives for the treatment of anxiety, produce sedation that lasts from twelve to twenty-four hours. Although no longer prescribed widely for that purpose, phenobarbital is one of the drugs used for the treatment of grand mal epilepsy. The short- and intermediate-acting drugs such as pentobarbital and secobarbital, which were once mainly employed as hypnotics, produce CNS depression that lasts for three to twelve hours, depending on the compound used. The ultra-short-acting barbiturates (e.g., thiopental) are used for the induction of anesthesia because of the ease and rapidity with which they induce sleep when given intravenously. The effects of barbiturates on judgment and other mental as well as motor skills, however, may persist much longer than the duration of the hypnotic effect. For this and other reasons, for the treatment of anxiety or insomnia, barbiturates have largely been replaced by the generally safer group of drugs called benzodiazepines.

The respiratory system is significantly depressed by the administration of barbiturate doses that are larger than those usually prescribed. Furthermore, there is a synergistic effect (i.e., one that is greater than simply adding the drugs' effects) when barbiturates are combined with alcohol and other central nervous system depressants—often with a fatal outcome. Barbiturates are frequently used for suicides. For this reason, too, barbiturates have been displaced by less toxic benzodiazepines. The symptoms of acute barbiturate toxicity resemble the effects observed after excessive alcohol ingestion. Although repeated administration of barbiturates results in CNS tolerance, thus producing less intoxication, tolerance does not appear to develop to the same extent for the respiratory depressant and lethal effects of the barbiturates; the person addicted to barbiturates may therefore be at a greater risk of respiratory toxicity

because of less pronounced CNS euphoric effects with higher doses, which may lead the individual to increase the dosage, resulting in respiratory depression. Tolerance to barbiturates also affects metabolism; the administration of these drugs speeds up not only their own metabolism (i.e., shortens their effectiveness) but also the metabolism of a large number of other drugs. This property has been of use in some special cases (as in jaundice of the newborn), but it can be hazardous in others when it decreases the effectiveness of another drug (e.g., an anticoagulant used to treat blood clots).

Long-term users experience withdrawal symptoms when the barbiturate is stopped abruptly. Abrupt cessation also leads to an increase in the amount and intensity of REM sleep (REM rebound). The intensity of the withdrawal symptoms varies with the degree of abuse and may range from sleeplessness and tremor in mild cases to delirium and convulsions in severe cases. Fatalities have occurred as a result of barbiturate withdrawal; this is more likely to occur with short-acting barbiturates. In some individuals, barbiturates may produce CNS excitement rather than CNS depression. This type of idiosyncratic reaction occurs most frequently in elderly people. Among the side effects sometimes seen, there may be rashes and muscle and body aches.

See also **Expectancies; Sleep, Dreaming, and Drugs.**

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BEERS AND BREWS. Beers and brews are beverages produced by yeast-induced fermentation of malted cereal grains, usually barley malt, to which hops and water have been added. They generally contain 2 to 9 percent ethyl alcohol, although some may contain as much as 15 percent. Various types and flavors are created by adding different combinations of malts and cereals and allowing the process to continue for varying lengths of time.

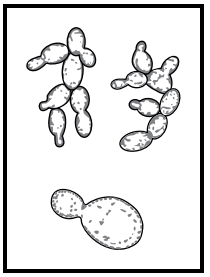

Figure 1. Yeast. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

BREWING HISTORY

The origin of beer is unknown, but it was an important food to the people of the Near East, probably from Neolithic times, some 10,000 years ago. The making of beer and of bread developed at the same time. In Mesopotamia (the ancient *land between the rivers* as the Greeks called it), an early record from about 5,000 years ago describing the recipe of the "wine of the grain" was found written in Sumerian cuneiform on a clay tablet. In ancient Egypt, at about the same time, barley beer was brewed and consumed as a regular part of the diet. It was known as *hek* and tasted like a sweet ale, since there were no hops in Egypt. Egyptians continued to drink it for centuries, although the name was changed to *hemki*. More than 3,200 years ago, the Chinese made a beer called *kiu* that was most likely made from two parts millet and one part rice. With water added, the concoction was heated in clay pots; flour and various plants were added to provide the yeast and flavors, respectively.

The ancient Greeks, however, preferred wine and considered beer to be a drink of barbarians. Beer was drunk on special occasions in ancient Rome; Plutarch wrote of a feast in which Julius Caesar served his officers beer as a special reward after they had crossed the Rubicon river. Once the art of brewing reached England, beers and ales became the preferred drink of the rich and poor alike. King Henry VIII of England was said to consume large quantities during breakfast. It was soon discovered that sailors who drank beer avoided scurvy, a disease caused by a lack of adequate amounts of Vitamin C. Thus, beer was added to each ship's provisions and was even

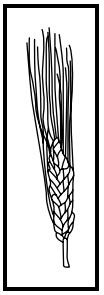

Figure 2. Barley. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

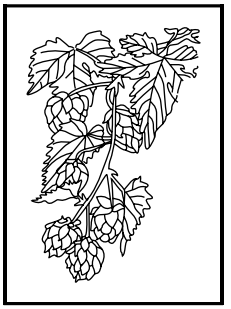

Figure 3. Hops. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

carried on the *Mayflower* during the crossing of the Atlantic Ocean in 1620. American colonists quickly learned to make their beer with Indian corn (maize), and much U.S. beer is still made with corn, although rice and wheat are also used in the mix with barley malt.

MAKING BEER

The first step in making beer is to allow barley to sprout (germinate) in water, a process that releases an important enzyme, amylase. Germinated barley seeds are called malt. Once the malt is crushed and suspended in water, the amylase breaks down the complex starch into more basic sugars. The reaction is stopped by boiling, and the concoction is filtered. This clear solution is mixed with hops (to provide the bitter flavor) and a starter culture of yeast (to begin the alcoholic fermentation process). Carbon dioxide gas (the fizz or bubbles) is produced, along with ethyl alcohol (ethanol or drinking alcohol). The malt and hops are then removed (and generally sold for cattle feed) while the yeast is skimmed off as fermentation proceeds. After the desired effect is achieved, the beer is filtered and bottled, or it is stored in kegs for aging. During the aging process (2 to 24 weeks) proteins settle to the bottom or are digested by enzymes. The carbonation (fizz) that occurred during fermentation is then drawn off and forced back in during the bottling process.

BEER TYPES

There are two major types of beers: top-fermenting and bottom-fermenting. Top fermentation occurs at room temperature 59° to 68°F (15°–20°C) and is so named because the yeast rises to the top of the vessel during fermentation. This older process produces beers that have a natural fruitiness and include the wheat beers, true ales, stouts, and porters. Their flavor is most completely expressed when served at moderate (i.e., room) temperatures. The development of yeasts that sank during this process resulted in brews that were more stable between different batches. Most of the major brewers have switched to the bottom yeasts and cold storage (lagering). The significance of using yeast that sinks during fermentation is that airborne yeasts cannot mix with the special yeast and contaminate the process.

The most popular type of beer in the United States is lager, a pale, medium-hop-flavored beer. It is mellowed several months at 33°F (0.5°C) to produce its distinctive flavor. Lager beers average 3.3 to 3.4 percent ethyl alcohol by weight and are usually heavily carbonated. Pilsner is a European lager (that originated in medieval Pilsen, now the Czech city of Plzen) that is stored longer than other lagers and has a higher alcohol content and a rich taste of hops. Dark beers are popular in Europe but are not generally produced in the United States. The dark color is achieved by roasting the malt; dark beer has a heavier and richer taste than lager beer. British beers are many and varied, both pale and dark; some have a number of unique additives, including powdered eggshell, crab claws or oyster shells, tartar salts, wormwood seeds, and horehound juice. Porter, popular in England, is another dark beer—originally called porter's beer, it was a mixture of ale and beer. The porters of today are a sweet malty brew and contain 6 to 7 percent alcohol. Malt liquors are beers that are made using a higher percentage of fermentable sugars, resulting in a beverage with 5 to 9 percent alcohol content; the mild fruity flavor has a spicy taste and lacks the bitterness of hops. Low-calorie (sometimes called "light" or "lite")

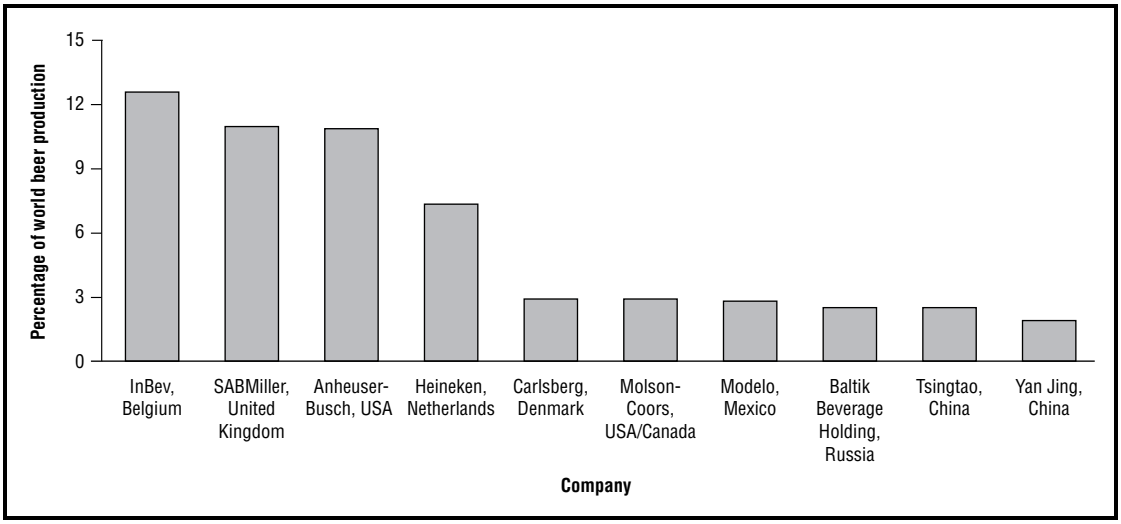

Figure 4. Top 10 brewing companies, 2005. (Adapted from Barth Report, 2005/2006, Barth Haas Group.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

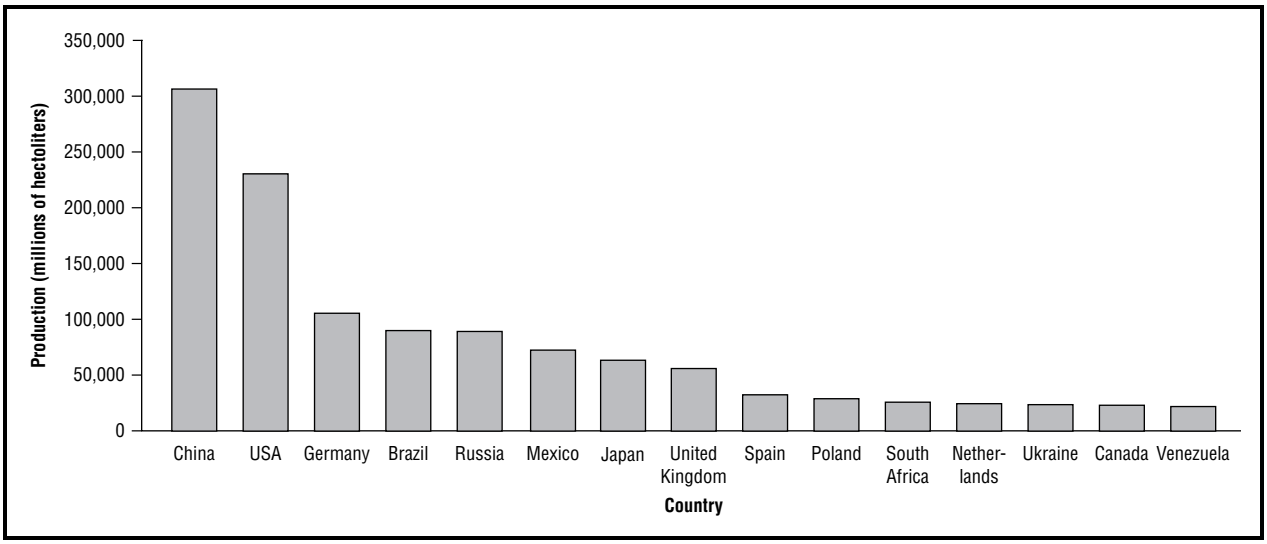

Figure 5. Top 15 beer-producing nations, 2005. (Adapted from Barth Report, 2005/2006, Barth Haas Group.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

beers are produced by decreasing the amount of grain used in the initial brew (using more water per unit of volume) or by adding an enzyme that reduces the amount of starch in the beer. These light beers contain only about 2.5 to 2.7 percent alcohol.

Brewing is subject to national laws concerning allowable ingredients in commercial products. Although chemical additives are allowed by some countries (e.g., the United States), German and Czech purity laws consider beers and brews a natural historical resource and disallow anything that was not part of the original (medieval) brewing tradition. Individuals sensitive to U.S. or Canadian beers are often able to drink pure beers.

See also **Alcohol: History of Drinking.**

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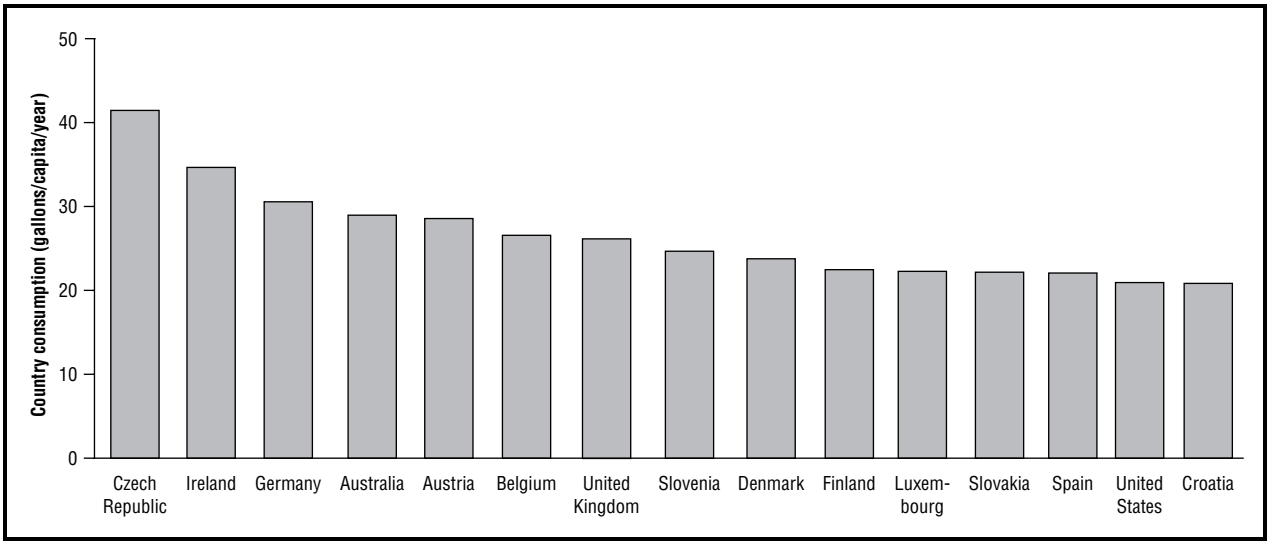

Figure 6. Top 15 beer-consuming nations, 2003. (Adapted from Kirin Holdings Company, Ltd.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

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BEHAVIORAL ECONOMICS.

Drug dependence can be conceptualized as a "syndrome in which the use of a drug is given a much higher priority than other behaviors that once had higher value" (Jaffe, 1990). Thus, understanding drug dependence requires understanding how drugs of dependence are valued and how the valuation of drugs changes in relation to other reinforcers. For example, individuals as they progress to addiction will engage in actions that jeopardize their employment, families, and health in pursuit of drugs.

This change in valuation can be understood through the field of inquiry referred to as behavioral economics. Indeed, the value of behavioral economics derives from its unique ability to quantify the valuation of qualitatively different reinforcers (Bickel et al., 1992; Bickel et al., 1995; Bickel & Vuchinich, 2000; Hursh, 1980, 1991) through the use of two conceptual and methodological approaches.

DEMAND

The first concept from behavioral economics to address this important issue is demand. The demand law refers to the observation that total consumption decreases as price increases, all else being equal (Allison, 1979). Price can be any number of manipulations (e.g., response requirement, monetary price, delay, changes in the amount of the commodity while holding the monetary or work price constant) that decreases the availability of a commodity. Indeed, drug self-administration studies that vary price (response requirement) report results consistent with the demand law; that is, drug consumption decreases as the response requirement increases (Griffiths et al., 1980; Young & Herling, 1986).

However, behavioral economics does more than simply restate this observation with a different terminology; it adds to it by quantitatively characterizing the relation between price and consumption via the economic measure of own-price elasticity (Bickel & DeGrandpre, 1996; Hursh & Bauman, 1987; Samuelson & Nordhaus, 1985). Own-price elasticity measures the proportional change in consumption across price conditions. If consumption of a particular reinforcer decreases proportionally to a large extent as price increases, then the consumption is referred to as elastic. If consumption decreases proportionally to a limited extent as price increases, then the consumption is referred to as inelastic. Elastic and inelastic consumption are quantified by elasticity coefficients greater than 1.0 and less than 1.0, respectively (Hursh, 1980). When examined across a broad range of prices, elasticity of demand for many reinforcers is often mixed: inelastic at low prices and elastic at higher prices.

With this method, then, qualitatively different reinforcers can be compared and distinguished in drug-dependent populations. For example, in one study, money and cigarettes were compared among cigarette-deprived subjects on progressive ratio schedules (Bickel & Madden, 1999; Bickel et al., 2000a). Response requirements were increased across sessions and the same response requirement was imposed separately for both commodities. At the lowest response requirements, money was self-administered to a greater extent than cigarettes (a greater intensity of demand). As response requirement increased, money was shown to be more sensitive to price than cigarettes. The own-price elasticities of money and cigarettes were 2.1 and 0.9, respectively, with money being 2.3-fold more sensitive to price. Such efforts can be meaningfully extended to clinical settings via simulation technology (Petry & Bickel, 1998; Jacobs & Bickel, 1999).

Jacobs and Bickel used questionnaires to assess the reported consumption of cigarettes and heroin separately and concurrently across a range of prices ($0.01 to $1,120) in opioid-dependent smokers undergoing treatment for heroin addiction. Across conditions in which cigarettes and heroin were available alone, or concurrently, demand for heroin was less elastic than for cigarettes. For example, heroin consumption was defended to a greater extent across increases in price than cigarettes. Taken together, these studies indicate that individuals with drug dependence value the primary drug of dependence more than other commodities. These observations also appear to have clinical utility. For example, in one study, MacKillop and Murphy (2007) used a hypothetical alcohol purchase task among college students who were consuming a high quantity of alcohol. These individuals received a brief intervention to reduce their alcohol consumption and those that demonstrated less sensitivity to price reported greater alcohol consumption six months after the intervention.

DELAY DISCOUNTING

A second concept from behavioral economics is delay discounting. Delay discounting measures the subjective value of a smaller immediate reinforcer versus a larger later reinforcer as a function of the delay (Rachlin et al., 1991). Delay discounting produces a quantitative value useful for assessing behavioral impulsivity: the inability to forgo immediate reinforcement in favor of a self-controlled option (Rachlin & Green, 1972). When applied to the field of drug dependence, delay discounting has been useful for identifying characteristics of drug abusers (Bickel & Marsch, 2001).

A typical delay discounting procedure asks a participant to make a series of judgments between two choices: an immediately available reinforcer or a larger delayed reinforcer. For example, participants are asked if they would rather be given $100 immediately or $1,000 after a 6-month delay. The value-immediate reinforcer is adjusted after each judgment until the participant is indifferent between the immediate and delayed reinforcer (Rachlin et al., 1991; Kowal et al., 2007). The process is then repeated for the same value of reinforcement at several delays: one day, one week, one month, one year, and so forth until a series of indifference points are generated. The measure can be administered orally using a series of cards (Rachlin et al., 1991), by pen and paper, or through a computer program (Johnson & Bickel, 2002).

The indifference points decrease in value as a proportion of the delay. Indifference points for each delay are used to fit a function that predicts choice

behavior. The standard fit for a discounting measure is Mazur's 1987 hyperbolic discount function:

$$v = \frac{V}{(1+k[D])}$$

In the Mazur function the discounted value (the value at which the individual is indifferent between immediate and delayed) is v, the undiscounted value (the value of the amount offered after the delay) is V, and D is the delay. Fitting the data to the function empirically derives the constant k; it represents the rate of discounting. Higher k values produce steeper discounting functions; that is, the higher the k the more likely an individual is to switch to the immediate reinforcer at a lower value. Thus, individuals who are more impulsive produce higher k values.

Delay discounting rates for delay to money reinforcers have been used to describe differences between a variety of forms of substance abusers and non-abusers. Individuals who use drugs make impulsive choices based on immediate reinforcement. A substance abuser forgoes long-term health, social, and economic benefits in favor of a short-term high. Steeper rates of discounting have been found between current smokers and never smokers (Bickel et al., 1999; Mitchell, 1999; Reynolds et al., 2004), light smokers and never smokers (Johnson et al., 2007), between abusers of alcohol and non-abusers (Petry, 2001; Richards et al., 1999; Vuchinich & Simpson, 1998;), between cocaine dependent and non-abusers (Coffey et al., 2003; Heil et al., 2006), and between opiate-dependent and non-abusing controls (Madden et al., 1999; Kirby et al., 1999; Madden et al., 1997).

Delay discounting rates are consistent with demand for specific commodities. Smokers, when offered the choice between a cigarette immediately and a number of cigarettes equivalent to larger sums of money later, discount cigarettes more steeply than money (Bickel et al., 1999; Baker et al., 2003). Heroin addicts discount heroin gains more steeply than money (Madden et al., 1997; Odum et al., 2000); alcohol abusers discount alcohol more steeply than money (Petry, 2001), and cocaine users discount cocaine gains more steeply than money (Coffey et al., 2003). When offered their preferred commodity, substance abusers show more difficulty choosing the self-controlled option, even when such choices are purely hypothetical. They almost singularly prefer a small amount of their preferred drug immediately to larger amounts available after a short delay.

This approach to studying delay discounting may have several important implications. First, rates of discounting may reflect and summarize the progression of addiction. Discounting rate increases when comparing controls to recently abstinent alcoholics to active alcoholics. Among smokers, the amount of nicotine consumed correlates directly with discounting rates (Ohmura et al., 2005; Johnson et al., 2007). Moreover, no difference in discount rates was found between ex-smokers (abstinent 1 year or longer) and never smokers (Bickel et al., 1999). Future work may address the relation of delay discounting and progression of addiction.

Secondly, delay discounting may have clinical utility similar to demand; that is, rate of discounting may predict relapse of a substance abuser seeking treatment. Yoon and colleagues (2007) measured discounting rates of women who spontaneously quit smoking while pregnant. Steep delay discounting rates predicted the likelihood that the woman would return to smoking in the post-partum session of the experiment. Similarly, among adolescent smokers attempting to quit, a similar measure of delay discounting using real money predicted successful abstinence in a contingency management program (Krishnan-Sarin et al., 2007). Additional research may expand this finding to all substance abuse disorders: steeper discounting rates coincide with poorer treatment outcomes. Collectively, these behavioral economic approaches provide a coherent and novel way to understand and measure drug dependence. Although more research is necessary, findings as of 2008 support the robustness and utility of this approach.

See also **Impulsivity and Addiction.**

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BEHAVIORAL TOLERANCE. In everyday language, tolerance implies the ability to withstand something. In pharmacology, the term *tolerance* is close to this meaning. To understand the technical meaning of the word, however, requires an understanding of the concept of the *potency* of a drug. A drug's potency is expressed in terms of the amount (the dose) of the drug needed to produce a certain effect. To illustrate, drugs may be compared with respect to potency. For example, relief from headache may be achieved with 650 milligrams of aspirin or with 325 milligrams of ibuprofen; in this case ibuprofen is said to be more potent, because less drug is needed to produce a particular effect (relief of headache). Tolerance is said to occur when a drug becomes *less potent* as a result of prior exposure to that drug. That is, following exposure (usually repeated or continuous administrations) to a drug, it may take more of the drug to get the same effect as originally produced.

The expression *behavioral tolerance* often is used simply to refer to a drug's decreased potency in affecting a specified behavior after repeated or continuous exposure to the drug. In other contexts, however, the expression has taken on a more restricted and special meaning; it is employed only when behavioral factors have been shown experimentally to have contributed to the development of tolerance.

This special meaning is applied when either of two sets of circumstances are encountered. In the first, drug tolerance is shown to be specific to the context in which the drug is administered; in the second, drug tolerance is shown to occur only if drug administration precedes particular behavioral circumstances. Examples of each may help clarify the distinctions between them and between "simple" tolerance and behavioral tolerance.

Context-specific tolerance has been researched extensively by Siegel and his colleagues (see Siegel, 1989, for an overview). In a typical experiment two groups of subjects are compared; subjects in both groups receive the same number of repeated exposures to the drug (e.g., morphine) and then are tested for their response to the drug (e.g., alleviation of pain). For one group, the test occurs in the environment where drugging took place; for the other the test occurs in a novel environment. Typically, only those from the group tested in the familiar environment show tolerance. Siegel's theory is that subjects develop, via the principles of Pavlovian conditioning, a conditioned compensatory response that is elicited by the drug-administration context—and that this response counteracts the effect of the drug (see Baker & Tiffany, 1985, for a different view). The phenomenon of context-specific tolerance helps explain why many overdoses of abused drugs occur when the drug is taken in a novel situation—the new context does not elicit compensatory responses that counteract the effects of the drug.

The importance of the temporal relationship between drug administration and behavior is illustrated by the phenomenon of "contingent" tolerance. The basic technique for identifying contingent tolerance was pioneered by Chen (1968), and a clear example is provided by Carlton and Wolgin (1971). Three groups of rats had the opportunity to drink milk for 30 minutes each day. For each group, injections of a drug or just a saline vehicle were made twice each day: For Group 1, each session was preceded by an injection of 2 milligrams per kilogram of amphetamine, followed by an injection of just the saline vehicle; for Group 2, the order of injections was reversed: saline before drinking, amphetamine after; Group 3 (the control group) received saline both before and after each session.

For Group 1 the drug initially decreased drinking, but during the course of several administrations, drinking recovered to control levels (i.e., tolerance developed). For Group 2, no effect on drinking was observed as a function of receiving the drug after sessions, so after several days (by which time subjects in Group 1 were tolerant) these subjects were given amphetamine before (rather than after) and saline after sessions (i.e., the conditions for Group 1 were implemented). Even though these subjects had received amphetamine just as frequently as the subjects in Group 1, when it was given before the session, drinking was suppressed just as much as it had been for Group 1 initially. Following repeated precession exposure to amphetamine the subjects in Group 2 became tolerant. These findings and many others like them show that, in many cases, for tolerance to develop to a drug's behavioral effects, mere repeated exposure to the drug is not enough. In addition, the drug must be active while the behavior of interest is occurring. (See Goudie & Demellweek, 1986, and Wolgin, 1989, for reviews.)

Contingent tolerance is sometimes called *learned* tolerance because it appears that it is a manifestation of learning to behave accurately while under the influence of a drug. An influential theory about the origin of contingent tolerance is the "reinforcement loss" theory of C. R. Schuster, W. S. Dockens and J. H. Woods (1966; for a review see Corfield-Sumner & Stolerman, 1978). Loosely stated, the theory is that contingent tolerance will emerge in situations where the initial effect of the drug is to produce a loss of reinforcement (e.g., result in a failure to meet the demands of the task). Although there are limits to the generality of the theory (Genovese et al. 1988), it has an excellent predictive record.

See also **Addiction: Concepts and Definitions; Reinforcement; Tolerance and Physical Dependence; Wikler's Conditioning Theory of Drug Addiction.**

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BENZODIAZEPINES. The benzodiazepines were introduced into clinical practice in the 1960s for the treatment of anxiety and sleep disorders. Members of this class of drug were classified initially as *minor tranquilizers* although this term has fallen into disfavor. These agents have proven to be safe and effective alternatives to older sedative-hypnotic agents such as barbiturates, chloral hydrate, glutethimide, and carbamates. Benzodiazepines are widely prescribed drugs, with 8.3 percent of the U.S. population reporting medical use of these agents in 1990.

BASIC PHARMACOLOGY

All benzodiazepines produce similar pharmacologic effects, although the potency for each effect may vary with individual agents. They decrease or abolish anxiety, produce sedation, induce and maintain sleep, control certain types of seizures, and relax skeletal muscles. The basic chemical structure is shown in Figure 1.

Dissimilarity in the effects of different benzodiazepines tend to be more quantitative than qualitative in nature. Many of these differences are attributable to how benzodiazepines are absorbed, distributed, and metabolized in the body. A few benzodiazepines—clorazepate for example—are pro-drugs; that is, they become active only after undergoing chemical transformation in the body. The extent to which a benzodiazepine is soluble in fatlike substances—that is, the degree to which it is lipophilic—determines the rate at which it crosses the tissue barriers that protect the brain. Drugs that are highly lipophilic such as diazepam (Valium) rapidly enter and then leave the brain. Benzodiazepines are metabolized in the body in a number of ways (see Table 1). Many benzodiazepines are transformed in the liver into compounds that possess pharmacologic activity similar to that of the originally administered drug. Diazepam, prazepam, and halazepam are all converted to the active metabolite desmethyldiazepam, which is eliminated from the plasma at a very slow rate. Oxazepam (Serax) and lorazepam (Ativan), in contrast, are conjugated with glucuronide, a substance formed in the liver, to form inactive metabolites that are readily excreted into the urine.

Most of the effects that result from the administration of benzodiazepines are a consequence of the

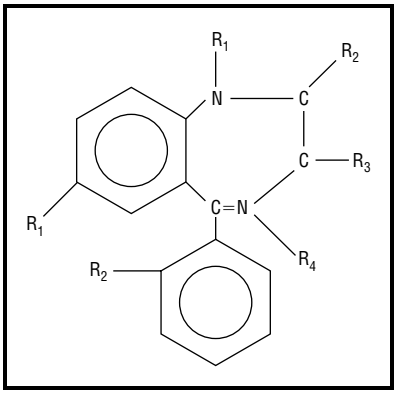

Figure 1. Outline of the basic structure of the benzodiazepines. R denotes substituent groups such as -H, -O, -OH, $-NO_2$, and -Cl that are attached to the core benzodiazepine structure. These groups determine the precise physiochemical and pharmacologic properties of each benzodiazepine. (Adapted from Rall, T.W. (1990). *Hypnotics and Sedatives: Ethanol.*) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Generic name	Trade name	Usual dose (mg/day)	Half-life (hours)	Transformation pathway	Metabolites (half-life, hours)
Anxiolytics					
Alprazolam	Xanax	0.75–4	8–15	Oxidation	Alphahydroxyalprazolam Benzophenone
Bromazepam			20–30	Oxidation	
Chlordiazepoxide	Librium	15–100	5–30		Desmethylchlordiazepoxide Demoxepam Desmethyldiazepam (36–96)
Clonazepam	Klonopin	1.5–20	18–50	Nitroreduction	Inactive 7-amino or 7-acetyl amino derivatives
Clobazam	Frisium	20–30	18	Oxidation	Desmethylclobazam (up to 77)
Clorazepate	Tranxene	15–60	30–100	Oxidation	Desmethyldiazepam (36–96)
Diazepam	Valium	4–40	20–70	Oxidation	Desmethyldiazepam (36–96)
Halazepam	Paxipam	60–160	14	Oxidation	Desmethyldiazepam (36–96) 3-hydroxyhalazepam
Lorazepam	Ativan	2–4	10–120	Conjugation	Inactive glucuronide conjugate
Oxazolam				Oxidation	Desmethyldiazepam (36–96)
Oxazepam[a]	Serax	30–120	5–15	Conjugation	Inactive glucuronide conjugate
Prazepam	Centrax	20–60	30–100	Oxidation	Desmethyldiazepam (36–96)
Hypnotics					
Brotizolam			4–7	Oxidation	
Estazolam	ProSom	1–2	8–24	Oxidation	
Flunitrazepam			10–40	Oxidation nitro-reduction	Desmethylflunitrazepam
Flurazepam	Dalmane	15–30	.5–3.0	Oxidation	Desalkylflurazepam (36–120) Hydroxyethyl flurazepam (1–4) Flurazepam aldehyde (2–8)
Lormetazepam			8–20	Conjugation	
Nitrazepam	Mogadon	2.5–10	20–30	Nitroreduction	
Quazepam	Doral	7.5–15	20–40	Oxidation	Oxoquazepam (25–35) Desalkylflurazepam (36–120)
Temazepam	Restoril	15–30	8–20	Conjugation	
Triazolam	Halcion	.125–.5	2–6	Oxidation	
Perioperative hypnotic					
Midazolam	Versed	1–2.5 mg/ml	1–4	Oxidation	Hydroxymethylmidazolam

Note: The half-life of a compound is the amount of time that must pass for the level of that agent in the plasma to be reduced by half.
[a]Oxazepam is also a metabolite of diazepam, clorazepate, prazepam, halazepam, and temazepam.

Table 1. Benzodiazepines available in the United States. (Adapted from *Drug Facts and Comparisons* (1994). St. Louis, MO: Facts and Comparisons. Greenblatt, D.J. (1991), Benzodiazepine hypnotics: Sorting the pharmacokinetic facts. *Journal of Clinical Psychiatry*, 52 (Suppl. 9), 4–10. Greenblatt, D.J., & Shader, R.I. (1987). Pharmacokinetics of antianxiety drugs. In H.Y. Meltzer (Ed.), *Psychopharmacology: The Third Generation of Progress*. NY: Raven Press.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

direct action of these agents on the central nervous system. Benzodiazepines interact directly with proteins that form the benzodiazepine receptor. Benzodiazepine receptors exist as part of a larger receptor complex (Figure 2). The interaction of the neurotransmitter gamma-amino butyric acid (GABA) with this complex leads to the enhanced flow of chloride ions into neurons (Kardos, 1993). This complex is referred to as the $GABA_A$ receptor-chloride ion channel complex. Much of the available evidence indicates that the action of benzodiazepines involves a facilitation of the effects of GABA and similarly acting substances on the $GABA_A$ receptor complex, thus leading to an increased movement of chloride ions into nerve cells. Entry of chloride ions into neurons tends to diminish their responsiveness to stimulation by other nerve cells, and consequently substances that produce an increase in chloride flow into cells depress the activity of the central nervous system. This depressant effect becomes manifested as either sedation or sleep. Agents that increase chloride ion inflow include not only the benzodiazepines but also other central nervous system depressant agents such as ethanol (alcohol) and the barbiturates. Benzodiazepines differ from barbiturates in that they require the release of GABA to affect the movement of chloride, whereas at higher doses barbiturates, through their own direct effects, can act to increase chloride inflow into cells.

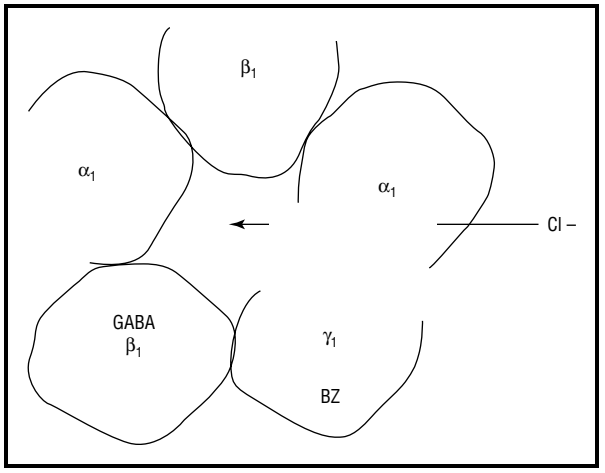

Figure 2. Schematic of one possible form of the $GABA_A$, receptor-chloride ion channel complex. Chloride ions enter through the center channel formed by alpha (α), beta (β), and gamma (γ) subunits. GABA receptors on β subunits regulate the flow of chloride ions through the channel. The activity of GABA receptors can be modulated by benzodiazepine receptors located on the γ subunit. (Figure created by Rebecca Bulotsky.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The $GABA_A$ receptor complex is composed of alpha, beta, and gamma subunits (Zorumski & Isenberg, 1991). Each subunit consists of a chain of twenty to thirty amino acids. Multiple subtypes of the alpha, beta, and gamma subunits have been shown to exist, and the types of subunits that form a single receptor complex appear to vary in different areas of the central nervous system. Some researchers have proposed that different drugs selectively interact with benzodiazepine receptors composed of a particular kind of α subunit, thereby leading to differences in drug effects. Although there is little evidence to support this hypothesis, future research should clarify the issue.

New compounds, such as the imidazopyridines, have been developed that act at the benzodiazepine receptor but are chemically distinct from the benzodiazepines. Zolpidem is an imidazopyridine used in clinical practice as a hypnotic agent. Other new drugs have been synthesized that can stimulate the benzodiazepine receptor but do not produce the maximal effects that result from the administration of higher doses of benzodiazepines. These drugs are classified as partial agonists. The drug abecarnil, which belongs to the beta-carboline class of compounds, is an example of such an agent that has been used experimentally to treat anxiety.

Flumazenil is a benzodiazepine derivative that has no activity of its own but acts to antagonize the actions of benzodiazepines at the benzodiazepine receptor. It is used to reverse the effects of these drugs during anesthesia or in benzodiazepine overdoses. Other compounds, including some of the beta-carbolines such as methyl-beta-carboline-3-carboxylate, act on the benzodiazepine receptor to produce effects that are opposite to those of benzodiazepines (Kardos, 1993; Zorumski & Isenberg, 1991). Administration of these inverse agonists can lead to the appearance of anxiety and convulsions.

THERAPEUTIC USE

Benzodiazepines are used for a variety of therapeutic purposes. Anxiety is the experience of fear that occurs in a situation where no clear threat exists. Numerous studies have demonstrated that anxiety disorders, including generalized anxiety disorder and many phobias, can be treated effectively with benzodiazepines. Panic disorder is a psychiatric illness in which patients experience intense sporadic attacks of anxiety often accompanied by the avoidance of open spaces and other places or objects that are associated with panic. High-potency benzodiazepines such as alprazolam (Xanax) or clonazepam (Klonopin) can prevent the occurrence of panic attacks in patients suffering from panic disorder. Flurazepam (Dalmane), triazolam (Halcion), and the other benzodiazepines listed in Table 1 are used in the treatment of insomnia and other sleep disorders. All rapidly acting benzodiazepines marketed in the United States have hypnotic effects. Classification of a benzodiazepine as a hypnotic is often more a marketing strategy than it is a decision based on pharmacologic differences among the class of drugs.

Status epilepticus is a seizure or a series of seizures that occurs over an extended period of time. This condition can lead to irreversible brain damage and is often successfully managed by the intravenous infusion of diazepam. Clonazepam is used either alone or in combination with other anticonvulsant medications to treat absence seizure and other types of seizure disorders. Clorazepate is used to control some types of partial seizures—that is, seizures that occur in a limited area of the brain. The increase in

central nervous system excitability, seizures, and anxiety that may appear during alcohol withdrawal can be treated with any benzodiazepine. Midazolam (Versed) is a benzodiazepine that is rapidly metabolized in the body and is used to help induce anesthesia during surgical procedures. The skeletal-relaxant properties of benzodiazepines make them useful for the treatment of back pain due to muscle spasms.

ADVERSE EFFECTS

Benzodiazepines have proven to be exceptionally safe agents. The dose at which these agents are lethal tends to be exceedingly high. Fatalities are more apt to occur when these drugs are taken in combination with other central nervous system depressant agents such as ethanol. Sedation is a common adverse effect associated with benzodiazepine use. Light-headedness, confusion, and loss of motor coordination may all result following the administration of benzodiazepines. Memory impairment may be detected in individuals treated with benzodiazepines, and this effect may prove to be particularly troublesome to elderly patients who are experiencing memory-related problems. Psychomotor impairment can be hazardous to individuals when they are driving. This problem can be exacerbated in individuals who consume ethanol while they are being treated with benzodiazepines. Hypnotic agents that are converted into active metabolites that are slowly eliminated from the body, such as flurazepam, may produce residual daytime effects that can impair tasks such as driving. The adverse effects of benzodiazepines on performance tend to be more of a problem in elderly people than in younger individuals. Patients with cirrhosis, a liver degenerative disease, are also more likely to experience benzodiazepine toxicity than are those with normal liver function. The appearance of the adverse effects associated with benzodiazepine administration in both elderly people and in cirrhotic patients can be minimized by treating them with agents such as oxazepam and lorazepam, which tend not to accumulate in the blood because they are excreted rapidly into the urine as glucuronide conjugates.

A small number of patients may exhibit paradoxical reactions when they are treated with benzodiazepines (Rall, 1990). These may include low-level anxiety, restlessness, depression, paranoia, hostility, and rage. Sleep patterns may be disrupted by benzodiazepine administration, and nightmares may increase in frequency. Benzodiazepines suppress two stages of the sleep cycle—the stage of deepest sleep, stage IV, and the rapid eye movement (REM) stage in which dreaming occurs.

TOLERANCE AND PHYSICAL DEPENDENCE

Tolerance to a drug involves either a decrease in the effect of a given dose of a drug during the course of repeated administration of the agent or the need to increase the dose of a drug to produce a given effect when it is administered repeatedly. Chronic treatment of animals with benzodiazepines leads to a reduction in potency of these agents as enhancers of chloride ion uptake. These effects at the cellular level are paralleled by the appearance of tolerance to the sedative effects of benzodiazepines. Tolerance also develops to the impairment of motor coordination that is produced by these drugs. Limited evidence suggests that the antianxiety effects of benzodiazepines may not diminish with time, or at the very least that benzodiazepines retain their effectiveness as antianxiety agents for several months.

Physical dependence results from adaptive changes in the nervous system that may be related to the development of tolerance. Dependence of this sort can be detected by the appearance of a characteristic abstinence or withdrawal syndrome when chronic administration of a drug is either abruptly discontinued or after the administration of an antagonist to the drug that has been taken for a prolonged period of time (Ciraulo & Greenblatt, 1995). Individuals who are treated chronically with benzodiazepines may exhibit signs and symptoms of withdrawal when the administration of these drugs is discontinued. Minor symptoms of withdrawal include anxiety, insomnia, and nightmares. Less common and more serious symptoms include psychosis, death, and generalized seizures. Signs of withdrawal may become evident twenty-four hours after the discontinuation of a benzodiazepine that is rapidly eliminated from the blood. Peak abstinence symptoms may not appear until two weeks after discontinuation of a benzodiazepine that is removed from the body slowly. Some of the symptoms that appear after benzodiazepine treatment is discontinued may be due to the recurrence of the anxiety disorder for which the drug had been originally prescribed.

In animals, the severity of withdrawal can be directly related to the dose and length of time of administration of a benzodiazepine. This kind of relationship has been harder to demonstrate in clinical studies. Many patients who are treated with benzodiazepines for prolonged periods of time may experience at least some symptoms of withdrawal, but most of these individuals should not be viewed as benzodiazepine "addicts" because they have relied on their medications for medical reasons, have taken the medications as directed by their physicians, and will not continue to compulsively seek out benzodiazepines once their prescribed course of treatment with these medications has been discontinued. The intensity of abstinence symptoms that may be seen in patients who are physically dependent on benzodiazepines can be markedly reduced if patients are allowed to gradually taper off their medications. There may be a risk of physical withdrawal from benzodiazepines in some patients who abruptly stop the medication following as few as four weeks after treatment. Patients who discontinue taking rapidly metabolized hypnotic drugs such as triazolam may be at risk for experiencing rebound insomnia, even if they have been under treatment for a few days to one week. Serious problems associated with benzodiazepine withdrawal are more likely to be a problem for patients who have been treated with high doses of these medications for four or more months.

ABUSE AND DEPENDENCE

Although no consensus exists as to the definition of drug addiction, diagnostic criteria for drug abuse and dependence have been developed by both the American Psychiatric Association and the World Health Organization. Drug abuse can be viewed as the use of a pharmacological substance in a manner that is not consistent with existing medical, social, or legal standards and practice. Alternatively, drug abuse has been defined in the Diagnostic and Statistical Manual of Mental Disorders of the APA as involving a "maladaptive pattern of substance use manifested by recurrent and significant adverse consequences related to repeated use" (American Psychiatric Association, 2000). Abuse of drugs may involve the use of drugs for recreational purposes—that is, drugs are administered to experience their mood-elevating (euphoric) effects. For some individuals, self-administration of drugs for these purposes may lead to compulsive drug-seeking behavior and other extreme forms of drug-controlled behavior. These behavior patterns may become further reinforced by the effects of withdrawal symptoms that dependent individuals attempt to reduce by the administration of the abused agent. The APA specifies that individuals can be classified as being drug dependent if they exhibit signs of drug tolerance, symptoms of withdrawal, cannot control their drug use, feel compelled to use a drug, and/or continue to use a substance even if the consequences of this use may prove harmful to them (American Psychiatric Association, 2000).

Abuse of drugs may sometimes represent self-medication. Cocaine and amphetamine users sometimes rely on benzodiazepines to relieve the jitteriness that may result from the administration of psychomotor stimulants. Some abusers of benzodiazepines may be medicating themselves with these agents to treat preexisting conditions of anxiety and depression.

The abuse liability of benzodiazepines—that is, the likelihood that they will be misused—has been assessed in studies of the tendency of either human beings or animals to administer these agents to themselves and studies of the subjective effects that result from the administration of different benzodiazepines. When provided access to cocaine and other psychomotor stimulants, animals will consistently self-administer these agents at high rates over time. Primates will intravenously self-administer benzodiazepines at moderate rates that are below those observed for the administration of barbiturates or cocaine. This finding and the results of a number of additional animal studies indicate that the benzodiazepines have a lower abuse liability than do the barbiturates or the psychomotor stimulants (Ciraulo & Greenblatt, 1995).

Individuals with a history of sedative-hypnotic abuse will self-administer triazolam and diazepam (Roache & Griffiths, 1989). In contrast, normal volunteers do not prefer diazepam to placebo. Subjective responses to drugs can be assessed through the use of instruments such as the Addiction Research Center Inventory-Morphine Benzedrine Group Scale and the Profile of Moods States that help to standardize the reports of subjects concerning their drug-induced experiences. Investigations in which subjective responses of normal subjects to benzodiazepine administration have been assessed indicate that these agents tend not to produce mood elevations in normal populations. On the other hand,

individuals with a history of either alcoholism or sedative-hypnotic abuse are more likely to experience euphoria after the administration of a single dose of either diazepam or other benzodiazepines. Adult children of alcoholics experience mood elevation after the ingestion of either alprazolam or diazepam, thus suggesting that these individuals may have a predisposition to benzodiazepine abuse.

Studies suggest that benzodiazepines are less likely to be abused than the barbiturates, opiates, or psychomotor stimulants, but that they carry more risk for abuse than do medications such as the anti-anxiety agent buspirone or drugs that have sedating effects such as the antihistamine diphenhydramine (Preston et al., 1992). There also may be differences among the benzodiazepines themselves. Some authorities believe that diazepam has greater abuse liability than halazepam, oxazepam, chlordiazepoxide, or clorazepate, although others believe that there is little difference among them. Diazepam, lorazepam, alprazolam, and triazolam all produce mood effects that are similar to those of known drugs of abuse. The rate at which these drugs reach the brain after administration may be a major determining factor in the onset of euphoria or pleasant effects associated with abuse. Inferences about abuse potential are made on the basis of subjective effects and self-administration in drug abusers and alcoholics. Many experts question the applicability of these findings to the general population.

Studies that accurately reflect the extent of benzodiazepine abuse in the United States are not available. A survey of American households produced by the National Institute on Drug Abuse suggested that the nonmedical use of tranquilizers was not a major health problem (Ciraulo & Greenblatt, 1995). Only 2.4 percent of individuals between the ages of 18 and 24 and 1.3 percent of survey respondents who were older than 26 reported using tranquilizers for nonmedical purposes. This type of survey does not take into account benzodiazepine usage among groups such as homeless people, prisoners, and migrant workers, and so it cannot convey a complete picture of how benzodiazepines are misused at the nationwide level (Cole & Chiarello, 1990).

Benzodiazepines are frequently used by individuals who abuse other drugs, but they are rarely used as either initial or primary drugs of abuse. Benzodiazepine abusers often take these drugs in combination with other agents. In Scotland, drug abusers have often injected temazepam in combination with the opioid drug buprenorphine (Ruben & Morrison, 1992). Large percentages of methadone-clinic patients have urine tests that are positive for benzodiazepines. Methadone-maintenance patients have indicated that diazepam, lorazepam, and alprazolam can produce desirable pleasurable effects (Sellers et al., 1993). Whether methadone patients use benzodiazepines to increase the effects of methadone or as self-medication for anxiety is not clear.

The percentage of alcoholics admitted for treatment who also concurrently use benzodiazepines ranges between 12 to 23 percent. High rates of benzodiazepine abuse have been found in alcoholics who have experienced failure in treatment programs for alcohol abuse. Clinical experience suggests that benzodiazepine abuse occurs with the greatest frequency in alcoholics with severe dependence and in alcoholics who abuse multiple types of drugs.

Individuals with a history of either alcohol abuse or alcohol dependence often have anxiety disorders. The issue of treating alcoholics with benzodiazepines is complex because some of these patients can take the medications without abusing them or relapsing to alcohol use whereas others take them in higher than prescribed doses and find that their desire to drink alcohol is increased.

BENZODIAZEPINES: SUMMARY

A large number of benzodiazepines are available for clinical use. These agents all share a set of pharmacologic properties that result from enhanced chloride flux at the $GABA_A$-receptor complex, which in turn results in the inhibition of neuronal activity in many regions of the central nervous system. Differences in activity among the benzodiazepines appear to be related primarily to differences in rates of absorption and metabolism, although recent research has suggested that intrinsic activity at benzodiazepine receptor subtypes also may influence drug effects. These drugs have been used extensively to treat anxiety, insomnia, seizures, and other disorders. They are safe and effective and their use has rarely been associated with irreversible adverse effects. Both physical and psychological dependence

may be problematic for some individuals who are treated on a long-term basis with these agents or who have abused alcohol or other drugs.

See also **Benzodiazepines: Complications; Sleep, Dreaming, and Drugs; Withdrawal: Benzodiazepines.**

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BENZODIAZEPINES: COMPLICATIONS.

Benzodiazepines have been widely used to allay anxiety and to induce sleep. Until the 1990s, they were believed to be both effective and extremely safe, but problems with these drugs started to become evident in the early 1980s. Since then, the medical profession in many countries has tried to inculcate a cautious attitude toward their prescription and use. Lay people and the media have also become increasingly critical of the widespread use of these medicines for apparently trivial indications. To understand these problems, some knowledge of various aspects of the different types and effects of these medicines is essential.

THERAPEUTIC USE OF BENZODIAZEPINES

Benzodiazepines are primarily used to lessen a patient's anxiety or to induce sleep. They also have other important uses, including the treatment of seizure disorders and skeletal muscle spasticity (e.g., cerebral palsy), as well as the management of alcohol withdrawal. They are also used with other drugs for the induction and maintenance of anesthesia during minor surgical procedures. Benzodiazepines include such drugs as chlordiazepoxide (Librium), diazepam (Valium), lorazepam (Ativan), and oxazepam (Serax). The term *benzodiazepine* describes a basic chemical structure common to all these medicines. Essentially, all these drugs work the same way and are differentiated mainly by their dose and duration of action. Some, like diazepam, are long acting and can be taken once daily; others, like lorazepam and alprazolam (Xanax), need to be taken more often. Many sleeping tablets (hypnotics) are benzodiazepines, and these include short-acting drugs such as triazolam (Halcion) and medium-acting drugs such as temazepam (Restoril).

An international survey done in the early 1980s showed that tranquilizers and sedatives of any type had been used at some time during the previous year by 12.9 percent of adults in the United States, 11.2 percent in the United Kingdom, 7.4 percent in the Netherlands, and 15.9 percent in France. Persistent long-term users comprised 1.8 percent of all adults in the United States, 3.1 percent in the United Kingdom, 1.7 percent in the Netherlands, and 5.0 percent in France. In a study conducted on elderly adults living in the United States in 1996, 7.5

percent were found to be taking anti-anxiety agents and 4.8 percent were using sedative-hypnotics (primarily benzodiazepines) (Aparasu, Mort, & Brandt, 2003). In another study of elderly adults living in the United States, 16 percent of new users of benzodiazepines continued to take the medication for up to 4 years (Gray et al., 2003). Generally, people starting tranquilizers have at least a 10 percent chance of going on to long-term use (more than 6 months). Some of these chronic users have chronic medical or social problems, and the tranquilizer blunts the unpleasant feelings of tension, anxiety, insomnia, and, to a lesser extent, depression.

UNWANTED (SIDE) EFFECTS

Side effects are reactions to drugs that are not therapeutic or helpful, and they are therefore unwanted. The most common side effects from taking benzodiazepines are drowsiness and tiredness, and these effects are most marked within the first few hours after large doses. Other complaints produced by benzodiazepines include dizziness, headache, blurred vision, and feelings of unsteadiness. The elderly are particularly sensitive to tranquilizers because of age-related changes in the way that the drugs are metabolized and excreted. These individuals may become unsteady on their feet or even mentally confused. The feelings of drowsiness are, of course, useful for inducing sleep.

With the longer-acting benzodiazepines, and with higher doses of medium-duration or short-acting drugs, drowsiness can still be present the morning after taking a sleeping tablet, and the drowsiness may even persist into the afternoon. Elderly persons are more likely to experience such residual, or "hang-over," effects. In those elderly individuals with cognitive deterioration or dementia (e.g. Alzheimer's Disease) a benzodiazepine may worsen symptoms of cognition and dementia. Older patients taking benzodiazepine sedatives are especially at risk of falls resulting in hip fractures, and they also are at an increased risk of being involved in a motor vehicle accident.

In addition to sedation, special testing in a psychology laboratory indicates that alertness, coordination, performance at skilled work, mental activities, and memory can all be impaired by benzodiazepines. Patients should be warned about these risks and advised not to drive or operate machinery, at least initially, until the effects of the benzodiazepine can be assessed and the dosage adjusted if necessary. If driving is essential to the patient's livelihood, small doses should be taken at first and the amount built up gradually under medical supervision. Judgment and memory are often impaired early in treatment, so important decisions should be deferred.

As with many drugs affecting the brain, benzodiazepines can interact with other drugs, especially alcohol. People taking tranquilizers or hypnotics should avoid drinking alcoholic beverages because the additive effects of these two central nervous system depressants can be dangerous. Other drugs whose effects may be enhanced include antihistamines (e.g., for hay fever), painkillers, and antidepressants. Cigarette smoking may lessen the effect of some benzodiazepines by promoting their more rapid breakdown by the liver.

Patients taking benzodiazepines may also show so-called paradoxical responses—or effects that are the opposite of those intended. For example, feelings of anxiety may be heightened rather than lessened, and insomnia may be intensified. Even more disturbing, patients may feel hostile and aggressive. They may engage in uncharacteristic criminal activities, sexual improprieties, or offenses such as soliciting sex or self-exposure, or they may show excessive emotional responses such as uncontrollable bouts of weeping or giggling. All of these are signs of the release of inhibitions, and they are also characteristic of alcohol effects in some people. Although these paradoxical effects may not last long, they necessitate stopping use of the benzodiazepine.

Benzodiazepines can affect breathing in individuals who already have breathing problems, such as those associated with bronchitis. Other side effects that may be occasionally encountered include excessive weight gain, rash, impairment of sexual functioning, and irregularities of menstruation. Benzodiazepines should be avoided during pregnancy whenever possible, as there may be a risk of congenital malformations to the fetus. When given during childbirth, benzodiazepines pass into the unborn infant and may depress the baby's breathing after birth. They also pass into the mother's milk and may sedate the suckling baby too much.

Many people have taken an overdose of a tranquilizer as a suicide attempt or gesture. Fortunately, these drugs are usually quite safe when taken alone, and the person generally wakes up unharmed after a few hours' sleep. However, if the benzodiazepine is combined with alcohol or another central nervous

system depressant, the outcome could be serious or even fatal.

There are more subtle side effects of benzodiazepines that can interfere in various ways with the treatment of the anxiety or sleep disorder for which they are used. These drugs lessen the symptoms of these problems, but they do not alter the underlying problem, whether it be an unhappy marriage, a precarious job, or some other situation. Indeed, by lessening the symptoms, the individual being treated may lose his or her motivation to identify, confront, and tackle the basic problems. Giving a benzodiazepine medicalizes the problem by making the nervous or sad person into a patient, implying that there is something physically wrong. Finally, some events like bereavement need "working through"—typically by grieving—but benzodiazepines can stop this normal process and actually prevent the bereaved individual from coming to terms with loss.

LONG-TERM EFFECTS OF BENZODIAZEPINES

It is not clear whether benzodiazepines and hypnotics continue to be effective after months or years of daily use. Undoubtedly, many patients believe that they continue to benefit by being less anxious or by sleeping better. After prolonged use, however, the effect of the drugs may be more to stop the anxiety or insomnia that stems from withdrawal than to combat any continuing, original anxiety. Most of the side effects lessen over time, a process known as *tolerance*. Some impairments, however, such as memory disturbances, may persist indefinitely, although patients usually come to terms with this, perhaps by resorting to written reminders.

A process called *rebound* occurs when stopping the drug makes the underlying condition worse. For a patient with insomnia, for example, benzodiazepines may improve sleep by inducing it more rapidly, making it sounder, and prolonging it. When the medication is stopped, rebound may occur on the following night or two, with the insomnia being worse than ever. Eventually, the rebound insomnia subsides, but the patient may have become distressed enough to resume the medication, thereby running the risk of indefinite use. The risk of rebound is greatest with short-acting benzodiazepines, especially in higher dose.

A similar problem follows stopping a daytime tranquilizer, particularly the benzodiazepine lorazepam. Anxiety and tension rebound to levels higher than those experienced on treatment, and often higher than the initial complaints. Tapering off the tranquilizer over a week or two lessens or avoids this complication. Rebound may even be seen in the daytime between doses of the tranquilizer. The patient, increasingly anxious as the effect of the earlier dose wears off, watches the clock until his or her next dose is due. Rebound may also occur later in the day after taking a short-acting sleeping tablet the night before.

ABUSE POTENTIAL

Only a few patients prescribed benzodiazepines push the dose up above recommended levels. If this happens, the user may become intoxicated, have slurred speech, and experience a lack of coordination. Some people with alcohol problems also abuse benzodiazepines. Intravenous (IV) injection of benzodiazepines and hypnotics has become an increasing problem and has led to controls on the manufacture and prescription of these drugs in various countries, including the United States and the United Kingdom. Some addicts abuse benzodiazepines alone; others combine it with heroin-type drugs. The injection of benzodiazepines can result in clotting of the veins. It also carries the risk of infectious diseases, such as hepatitis and HIV/AIDS, from sharing dirty syringes.

WITHDRAWAL

In withdrawal, symptoms occur that the patient has not previously experienced. These symptoms come on a day or two after stopping alprazolam or lorazepam, and a week or so after stopping diazepam or chlordiazepoxide. The symptoms rise to a crescendo and then usually subside over two to four weeks. In an unfortunate few, the symptoms seem to persist for months on end—a condition sometimes called *post-withdrawal syndrome*. The existence of this condition is disputed by some doctors, who ascribe the symptoms to a return of the original anxiety for which the drug was given.

Patients undergoing withdrawal commonly experience bodily symptoms of anxiety such as tremor, palpitations, dry mouth, or hot and cold feelings. Insomnia is usually marked, and some patients complain of unpleasant feelings of being out of touch with reality or with their own bodies. Severe headaches and

muscle aches and pains can occur, sleep is greatly disturbed, and there is a loss of appetite, leading to the loss of several pounds of weight. Disturbances of perception are characteristic of benzodiazepine withdrawal and include intolerance to loud noises or bright lights, numbness or a "pins and needles" sensation, unsteadiness, a feeling of being in motion (as on a ship at sea), and the experience of strange smells and tastes. Some people become quite depressed, and on rare occasions a patient may experience epileptic fits (seizures) or a paranoid psychosis (with feelings of persecution and loss of contact with reality).

Withdrawal symptoms are evidence of physical dependence; they show that the body has become so used to the effects of the drug that it cannot manage without it. When the drugs are discontinued, approximately one-third of long-term benzodiazepine users experience withdrawal, even when the tranquilizer or hypnotic is tapered off. Some users have tried to stop the medication and have encountered problems. Many others have never tried to stop and so are unaware that they are dependent. Because these people continue to take the doses prescribed by their doctors, it took the medical profession a long time to admit the scale of the problem. In addition, the similarity between some withdrawal symptoms and features of the original anxiety has led to confusion in the mind of both the patient and the doctor. True withdrawal symptoms, however, arise at a predictable time after stopping the benzodiazepine and are new experiences for the patient, while the old anxiety and insomnia symptoms are familiar to the patient and may return at any time, depending on external stresses.

Essentially, before discontinuing benzodiazepines, the patient must be prepared for withdrawal by being told what to expect. He or she should be taught other ways of combating anxiety, and withdrawal should be accomplished by gradually tapering off the dose over six to twelve weeks, or occasionally longer. Many people experience little or no upset, but a few undergo much distress. Sometimes substituting the long-acting diazepam in place of the short-acting lorazepam or alprazolam helps. Antidepressants may be needed if the patient becomes very depressed, but by and large, other drugs are unhelpful. Family and social support is essential. Usually, the family doctor can supervise the withdrawal quite safely, but occasionally specialist advice should be sought. A self-help group may also provide useful continued advice and support. It is important that benzodiazepines are never stopped abruptly, for there is a greatly increased risk of severe complications such as seizures or convulsions if this is done.

When they were first introduced, benzodiazepines were considered to be safe drugs, and they were prescribed widely and for long periods of time. They have now been shown to be potentially problematic medicines with undoubted benefits but definite risks. For short-term treatment in the severely anxious and sleepless, they are still useful—although other drugs are beginning to supplement and even supplant them. For the bulk of anxious people, though, nondrug treatments are increasingly popular.

See also **Addiction: Concepts and Definitions; Iatrogenic Addiction; Sleep, Dreaming, and Drugs; Tolerance and Physical Dependence.**

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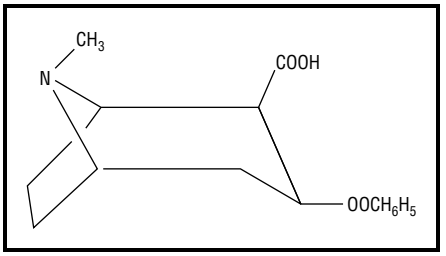
BENZOYLECOGNINE. Cocaine is metabolized by plasma and liver enzymes (cholinesterases) to water-soluble metabolites that are excreted in the urine. The two major metabolites are benzoylecognine and ecognine methyl ester, with only benzoylecognine reported to have behavioral activity. Since cocaine has a relatively short half-life and may only



Chemical structure of benzoylecognine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

be present in the urine for twenty-four to thirty-six hours, benzoylecognine levels in urine are useful markers of cocaine use, because its levels are present for a longer time in urine, two to four days, depending on the quantity of cocaine ingested. Assays for this metabolite are frequently employed in treatment programs, to evaluate compliance with the program, and in workplace drug testing to indicate cocaine use. Under these conditions, it is important to keep in mind that benzoylecognine in the urine is an indication of prior cocaine use, but reflects neither current use nor impairment.

See also **Cocaethylene: Immunologic, Hepatic, and Cardiac Effects; Cocaine; Drug Testing Methods and Clinical Interpretations of Test Results.**

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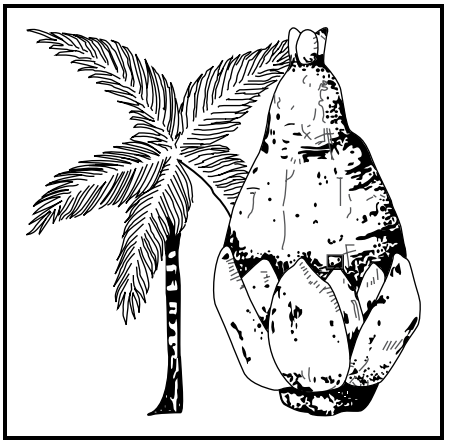
BETEL NUT. The betel or areca nut is the nut of the betel palm, *Areca catechu*, cultivated from eastern Africa to the South Pacific. Betel and its effects have been known throughout south and Southeast Asia at least since the time of Herodotus (fourth century BCE) as the palm is described in his work as well as in later writings in Pali and Sanskrit. Betel is thought to be the fourth most commonly used psychoactive substance in the world (after caffeine, nicotine, and alcohol), with the number of users estimated to be well into the hundreds of millions. Betel use is endemic, especially among aboriginal populations, from the Indian Ocean to the South Pacific. It is also commonly found in immigrant communities in the West. Betel is typically chewed like a chewing tobacco and the pigments in the nut color the saliva bright red. In a habitual user, these pigments may also dye the teeth red or black.



Betel palm and betel nut. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

CHEMICAL INTERACTIONS

The betel nut is commonly used in the form of a *quid*, which usually contains the nut itself, betel leaf, and slaked lime to extract the active alkaloids from the plant constituents of the quid. Betel leaf comes from the betel plant, *Piper betle*, which is distinct from the betel palm that produces the nut. Depending on the cultural context, other plants may be added, tobacco being the most common additive. Pharmacologically, the areca nut is the most important constituent of the quid, and the major psychoactive constituent is arecoline, an alkaloid with mild stimulant properties similar to those of nicotine in that it interacts with receptors for the neurotransmitter acetylcholine, although in a less specific fashion than nicotine. The immediate effects of betel chewing are euphoria, increased alertness, a sensation of warmth in the body, as well as increased salivation and sweating. The usual dose is a half nut. Two or more nuts are enough to produce severe side

effects or death. Like tobacco, and especially in combination with it (as in the south Asian gutka), areca chewing is addictive, although this remains a subject of some controversy. Also like tobacco, its use is associated with substantial health risks. Most habitual users will develop oral submucous fibrosis (OSF) within as little as five years. OSF involves a *bald tongue*, white lesions in the mouth, and an intolerance of spicy foods. Roughly 8 percent of those who develop OSF will go on to develop cancer. Betel chewing is implicated as a carcinogenic practice by the observation that as many as half of all malignant cancers in betel-chewing communities are oral cancers, most often oral squamous cell carcinomas.

CANCER RISKS

Although the association of cancer risk with tobacco use has received worldwide attention, those risks associated with betel preparations have not. This is particularly important to note, as it is evident that the likelihood of developing areca-associated cancers is higher than those associated with tobacco. Areca use, particularly in combination with tobacco, also seems to produce cancers much earlier than tobacco alone, which has led to a significant increase in the incidence of cancers in those under 50 in areas where the use of gutka-like betel preparations has become common. Gutka is a ready-made preparation of dried chopped betel nuts, various spices, and tobacco. It appears that gutka is particularly carcinogenic because of the addition of tobacco, which adds to both the carcinogenicity and to the addictive properties of the chew. Gutka is sold in stores and groceries throughout south Asia and in south Asian immigrant communities in other countries, most notably the United Kingdom. It is often packaged in bright containers with attractive labels and marketed to children as young as five years of age, all of which make gutka a particularly pernicious public health problem in those areas where it is in common use. In terms of positive effects, betel leaves and betel nut are used in a number of traditional medical systems, but scientific evidence of medicinal uses for the areca nut or its chemical constituents is minimal.

CULTURAL SIGNIFICANCE AND USES

As might be expected of a substance that has been used across such a large geographic area for thousands of years, its patterns of use and cultural significance are widely varied. In the Indian traditional medical systems of Ayurveda and Unani, betel has a number of uses in the treatment of digestive disorders and as a tonic, and similar uses are recorded in a number of other traditional systems. Betel has a number of cultural and ritual uses beyond its use as a stimulant. In Vietnam, the ceremonies surrounding marriage are referred to as "matters of betel and areca," and this association with marriage is also seen in India, Indonesia, and the Solomon Islands. In Malaysia and Melanesia, betel nuts are used for ritual purposes by magicians, both in love magic and as a poison. In India, the betel has many ritual uses and the palm itself is associated with Ganesha, lord of beginnings and remover of obstacles, which points to the cultural importance of betel in initiating and facilitating social interactions, much like the offer of a cigarette provides a point of entry for social interaction in other parts of the world.

The diversity of geographic and cultural milieus in which betel is used has not only led to a wide variety of cultural associations and uses of the nut and the palm itself, but has also spawned a wide variety of preparations of the betel for consumption. Betel wine is made in some regions, but betel is typically chewed. In most regions, the betel quid is the preferred form, although the nuts may also be raw, roasted, or fermented. In many cases, the quid is adulterated with other substances to enhance its flavor or effects. In south Asia, cardamom, cloves, and sandalwood are often added. The nut is also consumed chopped without betel leaf as paan masala, which is widely available in ready-made pouches in stores in south Asia and beyond. When tobacco is added to paan masala, it is referred to as gutka.

The cultural patterns of betel use are also complex and changing in response to the effects of immigration and the encroachment of a global culture. Among many aboriginal cultures of Southeast Asia and Oceania (e.g., Taiwan, and Malaysia and Papua New Guinea), betel use is associated with the maintenance of local tradition against the influx of immigrants and outside influence. In many of these situations, use by youth is increasing as a means of self-definition. In India and Taiwan, the use of betel by children has been on the rise in recent years. In most countries, however, where modern culture is viewed as more attractive, betel chewing is more the province

of the old. Similar dichotomies exist in the gender of users; in some cultures betel chewing is largely the province of women, as is the case in Cambodia, where women are more than 30 times more likely to be betel users than men. In other countries, such as Taiwan, it is principally a male habit.

The cultural trend that is the cause for greatest concern is the rise of widespread gutka use in south Asian communities. Most disturbing is the widespread use of gutka by children and adolescents, who are particularly vulnerable to tobacco addiction and more than likely vulnerable to the habit-forming properties of betel as well. In some parts of India, as many as 50 percent of children have a betel-chewing habit, a statistic that is likely to have an enormous impact on the health system of that nation as they develop OSF and cancer. This is also likely to be a problem in those Western countries with large numbers of south Asian immigrants, as areca nut use is totally unregulated and doctors and public health authorities are unfamiliar with the diseases it is likely to produce. Furthermore, the rate of betel use among immigrant communities may actually be higher than the rate in their home country, as one study found that as many as 80 percent of adult Bangladeshis living in London were regular betel users, as compared to a rate of 20 to 40 percent across the south Asian region (Gupta & Ray, 2004). In the Indian state of Kerala, authorities have gone so far as to ban the sale of smokeless tobacco, and similar proposals have been made at the national level. However, the use of betel without tobacco is likely to remain deeply ingrained in those cultures where it has been used for millennia, and with that use a heightened level of oral cancers will persist.

The future of betel use is likely to show complex patterns, not unlike those of tobacco use, which is declining in the West but rising in countries like China. In many regions of Asia, betel use seems destined to decline over the foreseeable future, as public health authorities become more vocal about the risks and populations discard the traditions associated with betel use for the attractions of modern global culture. The possibility exists that betel use might spread to cultures unfamiliar with its use and even less familiar with its risks, but the hope is that regulations against its use by children and adolescents may be promulgated to minimize potential harm in both new and old populations of betel users.

See also **Plants, Drugs From.**

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BHANG. This is one of the many names given to the hemp plant, *Cannabis sativa*, and its products. Bhang is of Hindi origin (from *bhãg*, which came into English about 1563) and refers to the leaves and flowering tops of uncultivated hemp plants. In 1895, the Indian Hemp Commission took the position that bhang was not a major health hazard. Bhang is taken in a beverage in India called *thandaii*, may be served in sweetmeats, or is used in making ice cream. It is often served at weddings or religious festivals and is freely available from sidewalk stands in the major cities. Generally, in India, the use of bhang and other cannabis products has been considered lower class. Probably as a result of continuing British-based influence, the upper-class drugs are alcohol and opium.

See also **Cannabis Sativa; Marijuana (Cannabis); Plants, Drugs From; Slang Terms in U.S. Drug Cultures.**

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BLOOD ALCOHOL CONCENTRATION. The consumption of alcoholic beverages results in the absorption into the bloodstream of alcohol (ethanol, also called ethyl alcohol) from the stomach and small intestine. The amount of alcohol distributed in the blood is termed blood alcohol concentration (BAC) and is proportional to the quantity of ethanol consumed. It is expressed as the weight of alcohol in a fixed volume of blood, for example, grams per liter (g/l) or milligrams per

deciliter (mg/dl). The measurement of blood alcohol concentrations has both clinical and legal applications.

The most important factors that determine BAC are the presence of food in the stomach, the concentration of alcohol consumed, the rate and volume of alcohol consumed, and gender. Consuming food with alcohol generally decreases the volume of alcohol that can be quickly absorbed into the bloodstream. This is more evident for small volumes of more concentrated alcohol such as hard liquor than for larger volumes such as beer, a lower concentrated form of alcohol. Consuming more than one drink per hour causes the BAC to increase rapidly because it typically exceeds the rate at which the body can metabolize alcohol. The percentage of body fat that contributes to a person's total weight also affects BAC. A larger proportion of fat provides less body water into which the alcohol can distribute, thus increasing BAC. For this reason, women generally have a higher BAC for a given number of drinks when compared to men, even when accounting for the difference in body weight associated with sex.

See also **Alcohol.**

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BLOOD ALCOHOL CONCENTRATION, MEASURES OF.

The first analytical methods for measuring alcohol (ethanol) in blood and other body fluids were developed in the nineteenth century. Although by modern standards these pioneer efforts were fairly crude, they were sufficiently reliable to establish a quantitative relationship between blood-alcohol concentration (BAC) and the various signs and symptoms of inebriation. A significant advance in methodology came in 1922 when Erik M. P. Widmark published his micro-method for analyzing ethanol in specimens of capillary blood.

WIDMARK METHOD

In Widmark's day the small amounts (aliquots) of blood needed for each analysis could be measured more accurately by weight than by volume, since constriction pipettes were not yet available. Widmark therefore weighed the amount of blood required to the nearest milligram (0.001 g) with the aid of a torsion balance. He then reported the results of ethanol determinations in terms of mass per mass units, actually milligram of ethanol per gram of whole blood (mg/g), sometimes referred to as *per mille* (meaning, *parts per thousand*). This way of reporting BAC survives today in Scandinavian countries where Widmark's method became widely used for legal purposes.

LATER BAC METHODS

Modern methods of ethanol analysis (such as gas chromatography) plus the availability of modern clinical laboratory equipment made it more convenient to dispense the aliquots of blood needed for analysis by volume rather than by weight. Micropipettes and more recently diluter-dispenser devices are now widely used for dilution of blood prior to the analysis. The term *concentration* has little meaning when used alone, because it can be expressed in many different ways. The choice of units for reporting BAC differs among countries: for example, milligrams per hundred milliliters (mg/100 ml) in Great Britain (unfortunately often appearing as the ambiguous

Concentration unit	Country	Legal limit	g/100ml
Percent weight/ volume (% w/v)	United States*	80mg /100 ml	0.08 g/100 ml
Milligrams per 100 milliliter (mg/dl)	Britain	80 mg/100 ml	0.08 g/100 ml
Milligrams per milliliter (mg/ml)	Netherlands	0.50 mg/ml	0.05g/100ml
Milligrams per gram (mg/g)***	Sweden**	0.20 mg/g	0.02g/100ml
Milligrams per gram (mg/g)	Norway**	0.50 mg/g	0.05g/100ml

*The Uniform Vehicle Code of the National Committee on Uniform Traffic Laws and Ordinances recommends 0.08 grams per 100 milliliters of blood or per 210 liters of breath; all U.S. states have adopted this recommendation.
**1 milliliter whole blood weighs 1.055 grams.
***Conversion of weight/weight measurement is approximate

Table 1. Concentrations of alcohol (ethanol) in whole blood for legal purposes. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

State	BAC defined as illegal per se (mg/dl)	Administrative license suspension 1st offense	Restore driving privileges during suspension?	Do penalties include interlock/ forfeiture?*	DUI related fatalities in 2006
Alabama	0.08	90 days	No	No/No	475
Alaska	0.08	90 days	After 30 days	Yes/Yes	23
Arizona	0.08	90 days	After 30 days	Yes/Yes	585
Arkansas	0.08	120 days	Yes	Yes/Yes	254
California	0.08	6 months	After 30 days	Yes/Yes	1,779
Colorado	0.08	3 months	After 30 days	Yes/No	226
Connecticut	0.08	90 days	Yes	No/No	129
Delaware	0.08	3 months	No	Yes/No	57
District of Columbia	0.08	2–90 days	Yes	Yes/No	18
Florida	0.08	6 months	After 30 days	Yes/Yes	1,376
Georgia	0.08	1 year	After 30 days	Yes/Yes	604
Hawaii	0.08	3 months–1 year	After 30 days	No/Yes	84
Idaho	0.08	90 days	After 30 days	Yes/No	106
Illinois	0.08	3 months	After 30 days	Yes/Yes	594
Indiana	0.08	180 days	After 30 days	Yes/Yes	319
Iowa	0.08	180 days	After 90 days	Yes/No	148
Kansas	0.08	30 days	No	Yes/No	170
Kentucky	0.08	—	—	Yes/No	272
Louisiana	0.08	90 days	After 30 days	Yes/Yes	475
Maine	0.08	90 days	Yes	Yes/Yes	74
Maryland	0.08	45 days	Yes	Yes/No	268
Massachusetts	0.08	90 days	No	Yes/No	174
Michigan	0.08	—	—	Yes/Yes	440
Minnesota	0.08	90 days	After 15 days	Yes/Yes	183
Mississippi	0.08	90 days	After 90 days	Yes/Yes	375
Missouri	0.08	30 days	No	Yes/Yes	500
Montana	0.08	—	—	Yes/Yes	126
Nebraska	0.08	90 days	After 30 days	Yes/No	89
Nevada	0.08	90 days	After 45 days	Yes/No	186
New Hampshire	0.08	6 months	No	Yes/No	52
New Jersey	0.08	—	—	Yes/No	341
New Mexico	0.08	90 days	After 30 days	Yes/No	186
New York	0.08	Variable	Yes	Yes/Yes	558
North Carolina	0.08	30 days	After 10 days	Yes/Yes	554
North Dakota	0.08	91 days	after 30 days	Yes/Yes	50
Ohio	0.08	90 days	after 15 days	Yes/Yes	488
Oklahoma	0.08	180 days	Yes	Yes/Yes	263
Oregon	0.08	90 days	After 30 days	Yes/Yes	196
Pennsylvania	0.08	—	—	Yes/Yes	600
Rhode Island	0.08	—	—	Yes/Yes	42
South Carolina	0.08	30 days	Yes	Yes/Yes	523
South Dakota	0.08	—	—	No/No	80
Tennessee	0.08	—	—	Yes/Yes	509
Texas	0.08	90 days	No	Yes/Yes	1,677
Utah	0.08	90 days	No	Yes/No	69
Vermont	0.08	90 days	No	No/Yes	29
Virginia	0.08	7 days	No	Yes/Yes	379
Washington	0.08	90 days	After 30 days	Yes/Yes	294
West Virginia	0.08	6 months	After 30 days	Yes/No	161
Wisconsin	0.08	6 months	Yes	Yes/Yes	364
Wyoming	0.08	90 days	Yes	No/No	80
Puerto Rico	0.08	—	—	—	215

*A multiple offender's vehicle may be seized and disposed.

Table 2. States legal limits for blood alcohol concentration (BAC) level. (Source: Traffic Safety Facts, 2006. National Highway Traffic Safety Administration, U.S. Department of Transportation.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

mg%), gram percent weight per volume (g% w/v) in the United States, and milligrams per milliliter (mg/ml) in many European countries. Other ways of reporting BAC in clinical medicine are milligrams per deciliter (mg/dl), grams per liter (g/liter), or micrograms per liter (μg/liter). When countries outside Scandinavia enacted legal limits for ethanol in the blood of motorists, the concentrations were defined in units of mass of ethanol per unit volume; whether it was grams, milligrams, or micrograms of ethanol in a volume of milliliters, deciliters, or liters seems chosen arbitrarily.

BAL (mg/dl)	(BAC)	Effects
50	(0.05%)	There may be no observable effects on behavior, but thought, judgment, and restraint may be more lax and vision is affected. Significantly more errors in tasks that require divided attention; more steering errors; and increased likelihood of causing an accident.
80	(0.08%)	Reaction time for deciding and acting increases. Motor skills are impaired. The likelihood of a crash increases to three to four times the likelihood when sober.
100	(0.10%)	Six times as likely to be involved in a crash. Reaction time to sights and sounds increases. Physical and mental coordinations are impaired: Movement becomes noticeably clumsy.
150	(0.15%)	Twenty-five times as likely to be involved in a crash. Reaction time increases significantly, especially in tasks that require divided attention. Difficulty performing simple motor skills. Physical difficulty in driving.
200	(0.20%)	One hundred times as likely to be involved in a crash. Motor areas of brain significantly depressed, and all perception and judgment distorted. Difficulty standing, walking, and talking; driving erratic.
300	(0.30%)	Confusion and stupor; inability to track a moving object with the eyes. Passing out is likely.
400	(0.40%)	Coma is likely.
450–500	(0.45%–0.50%)	Death is likely.

Table 3. Effects of blood alcohol levels. (Source: Adapted from Mothers Against Drunk Driving (MADD) and the National Safety Council.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Because the specific gravity of whole blood is greater than water (on average, 1 ml of whole blood weighs 1.055 g), BAC expressed in terms of mass per mass (w/w) is not the same as mass per volume (w/v). In fact, a concentration of 0.10 percent w/v equals 0.095 percent w/v. This difference of about 5.5 percent could mean punishment or acquittal in borderline cases of driving while under the influence of alcohol. With the *per se* ethanol limits in U.S. states, great care is needed to ascertain whether w/v or w/w units were intended by the legislature when the statute was drafted. Table 1 gives examples of the statutory limits of breath-ethanol concentrations commonly used to report BAC for legal purposes in several countries.

If ethanol were determined in plasma or serum, the concentration would be about 10 to 15 percent higher than for the same volume of whole blood, because there is more water in the sample after the erythrocytes (red blood cells) are removed.

SI MEASUREMENTS

In clinical chemistry laboratories, the Système International d'Unités (SI) has gained worldwide acceptance. According to the SI system, the amount of substance implies *mole* rather than mass. The mole, or a submultiple thereof, replaces mass units such as grams or milligrams. Accordingly, the concentration of a substance of known molecular weight might appear as mole/liter or millimole per liter (mmol/l) or micromole per liter (μmol/liter). Note that liter is the preferred unit of volume when reporting concentrations of a substance in solution in the SI system. The molecular weight of ethanol is 46.06, and therefore a concentration of 1.0 mol/l corresponds to 46.06 g of ethanol in 1 liter of solution. Likewise 1.0 mmol/l contains 46.06 mg; 1.0 μmol/l contains 46.06 μg, and so on. Publications in the field of biomedical alcohol research often report BAC in this way. It follows that 0.1 g percent w/v or 100 mg/dl is the same as 21.7 mmol/l.

CONVERSION OF BREATH TO BLOOD ETHANOL

Statutory limits of BAC existed in several countries before methods of analyzing the breath were developed. It therefore became a standard practice to convert the concentration of ethanol measured in the breath (BrAC) into the presumed concentration in the blood. For this purpose, a conversion factor, usually 2,100:1 was used. Presumably, it was less troublesome to make this conversion than to rewrite the statute to include both BAC and BrAC as evidence of impairment. Accordingly, breath-ethanol analyzers were calibrated in such a way that the readout was obtained directly in terms of the presumed BAC. This conversion of breath to blood ethanol

created the dilemma of a constant blood/breath ratio existing for all subjects under all conditions of testing. In the United States and elsewhere, a blood/breath factor of 2,100:1 was approved for legal purposes with the understanding that this gives a margin of safety (about 10%) to the accused. Indeed, more recent research suggests that the blood/breath factor should be 2,300:1 for closer agreement between direct BAC and the result derived from BrAC. In the Netherlands and Great Britain, 2,300:1 was chosen as the legal limit of BrAC when evidential breath-ethanol analyzers were introduced.

Both the prescribed BAC or BrAC limits for motorists and the units of concentration differed among countries and even within regions of the same country. The notion of reaching an international agreement about one common BAC or BrAC limit for motorists is an attractive one, but hardly attainable.

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BOLIVIA. Bolivia is a landlocked nation situated in the central part of South America. Bolivia's 424,165 square miles has an estimated population of 9,247,816 as of July 2008. The ethnic breakdown of the population becomes crucial for understanding the political dynamics and the role of the coca/cocaine trade in the region: white, 15 percent; Aymara Indians, 25 percent; Quechua Indians, 30 percent; and mestizos (mixed white and Amerindian), 30 percent. Bolivia is rich in mineral resources, having deposits of petroleum, natural gas, tin, lead, zinc, copper, silver, and gold. Since the early sixteenth-century Spanish Conquest of South America, the resources have been in the hands of a European elite, with indigenous peoples largely becoming landless peasantry. Approximately 70 percent of the population lives in the Altiplano region, where the climate is less harsh than in the higher mountains. The other 30 percent, primarily Inca descendants, reside in the Yungas, Chapare, and Beni regions where coca plants (Erythroxylum coca) are cultivated.

The conquest and colonial rule were traumatic experiences for the Inca. Easily susceptible to European diseases, the native populations succumbed to tuberculosis, smallpox, and influenza. Combined with the harsh colonial systems of rule, the population decreased significantly following Spanish Conquest. The Inca populations also diminished due to the introduction of the mita obligations. *Mita* is a Quecha word meaning *turn* or *time*; the word was used to describe a forced-labor draft imposed by the Spanish on indigenous people. Native men were forced to labor for one year out of every six for Spanish rulers. Among the Inca, there had been a mita system that was reciprocal in the sense that in return for labor, the leader provided appropriate remuneration, land to grow food, acceptable working conditions, and health care. However, under Francisco de Toledo (c. 1515–1584), a Spanish viceroy of the area (1569–1581), the Mita system was both exploitive and racist. The Incas were worked to exhaustion in the mines with no ability to effectively challenge the conditions. A new form of slavery arose in which the Spanish set impossible work quotas to ensure that the workers remained forever in debt. Effectively, generations of young men were worked to death. The Spanish forced indigenous servitude in the mining industry. The local populations resorted to substance use as one way to cope with their deteriorating conditions.

Between 1556 and 1780, Potosi, located in south-central Bolivia, became one of the largest and richest cities in the world. In addition to the riches pooled from mining, the Catholic Church levied a 10 percent tax on coca leaves, and the income ensured the building of churches and Catholic schools. Thus in industry and through the imposition of the Catholic Church, local peoples were impoverished and decimated.

HISTORY OF COCA

The coca plant is integral to the Bolivian economy and was used by native inhabitants prior to the Spanish Conquest. The Spanish focused first on local mineral wealth. Initially they had little understanding

of coca as there was no equivalent plant in the Old World. Within a year following the rediscovery of silver at Potosi (the Incas had already known of the deposits) and the Spanish exploitation of indigenous labor, approximately seven thousand Incas were working local mines. As mines went deeper the Incas relied increasingly on chewing coca leaves. By 1548 the miners were chewing over a million kilos per year.

The capital city La Paz arose in response to the coca and silver trade. Coca was brought there to be auctioned, and silver merchants rested there before embarking on their journey to the coast and on to Spain. Thus, the coca and mining industries were linked. In 1552 the Catholic Church petitioned Charles I of Spain (also known as Charles V, Holy Roman Emperor). This petition was resolved at the First Council of Lima, where for the first time coca chewing was perceived as ruining the health of the Inca people. The Church emphasized the plant's intoxicating effect, but no concern was expressed regarding the mortality rates in the silver mines. The Church likened the opiate effects to demonic possession as it sought to supplant perceived pagan beliefs with Catholic ones. Coca was linked to a pre-Christian past. But coca suppression became a political problem for the colonists when the Incas refused to work in the mines without the drug. To make matters more complicated, the Incas were used to being paid in coca leaves. In the end, the Spanish authorities decided not to suppress the coca industry for economic reasons.

The discovery of mercury at Huancavelica in 1571 entailed the extension of the mita system to the mercury mines. Mercury was used in extracting silver from ore and increased the yield but was extremely toxic for workers. A far higher death rate occurred at Huancavelica than at Potosi. Few Incas completed the one year of labor conscription. Those miners who were sustained by coca chewing were thus exploited both by the colonial monopoly of the drug and the slave system of forced mining labor.

The mita system lasted until the early nineteenth-century Bolivarian Revolution, which transformed South America from European colonialism to independent states. The revolutionary Simón Bolívar (1783–1830) wished to establish liberty based upon the progressive ideas of the United States, but this vision was thwarted by internal divisions. The large landowners perceived an opportunity to establish states based upon their own interests. Therefore, the legacy of the revolution left the land in question largely untouched. The soldiers who had been provided with land bonds sold them to landowners, which created a greater concentration of land in the hands of a few European families until the land reforms in the 1950s. The society stratified economically and racially was reduced to white European and Creole families controlling the large estates and various Inca tribes providing the labor necessary to maintain them.

Wealth accumulated in the hands of a few. By 1900 José María Gamarra, the so-called coca king, dominated the Bolivian market; he owned 32 percent of all the haciendas in the Yungas region. The owners of the cocaine-producing haciendas formed the Sociedad de Propietarios de Yungus e Inquivisi (Society of Yungas and Inquivisi) (SPY) in 1830. The primary aim of the society was to ensure the hacienda coca growers had a voice in Bolivian politics. They also wanted to promote the use of coca in the urban centers. When the second opium convention took place in Geneva in 1925 cocaine was included as part of the League of Nations debate on narcotics. The plant was seen by Bolivians as integral to the national psyche and this was the argument put forward by the Bolivian representative.

The Bolivian government's official position was influenced by SPY. Prior to the 1949 UN conference on illicit drugs, SPY'S strategy was to highlight the nutritional value of coca chewing as well as its medicinal qualities. The United Nations Report of 1950, following an investigation of the conditions in Bolivia, concluded coca chewing did not have any nutritional value. The authors also noted coca chewing was extensive among the malnourished native populations, who were not eating properly because they were spending their income on coca chewing. The 1950 UNODC report undermined the various SPY arguments that coca chewing helped with altitude sickness and had nutritional and medicinal value. Instead, the report highlighted Indian populations that chewed coca to combat the physical and psychological effects of poverty.

GOVERNMENTAL FACTORS AND THE COCAINE INDUSTRY

Land reform, which occurred in 1952 following the victory of the National Revolutionary Movement (MNR), resulted in many large haciendas being subdivided and the land being given to the peasants. Land reform initially reduced reliance on coca for many people. Following land distribution the peasants had the ability to grow crops for food. Coca plantations were replaced with coffee as a cash crop as Bolivia entered the international market. Some people believe that with the alleviation of poverty and stress in the 1950s and 60s, coca chewing declined. However, political unrest contributed to cocaine once again becoming important in the national economy. A military junta replaced the National Revolutionary Movement (MNR) in 1964. The junta ruled until 1969 when elections were allowed and a leftist, Juan José Torres, was elected president. As he aligned Bolivia with Chile and Cuba, Bolivia became increasingly unstable and cocaine rose in importance.

In 1971 Hugo Bánzer, supported by the CIA, forcibly ousted President Torres in a coup. Bánzer employed Klaus Barbie (1913–1991), the former Nazi head of the Gestapo in Lyons, known as the Butcher of Lyons, who assisted the fledgling junta by using terror to silence opposition. He also orchestrated the cocaine trade through his shipping company Transmaritania. This activity marked a significant change in Bolivia as the government was now officially involved in cocaine production and distribution. Bánzer had encouraged landowners to grow cotton as a cash crop to sustain the Bolivian economy, but the price of cotton collapsed. As Bolivian cocaine production increased, the price fell from $1,500 per gram to $200 per gram in the United States.

Hugo Bánzer left office in 1978 after his wife was caught smuggling cocaine into the United States. In 1979 Barbie and Roberto Suárez, a cocaine smuggler, orchestrated another army coup. Union leaders were shot, universities were closed, printing presses were firebombed, and mass executions were carried out in the La Paz football stadium. Barbie and Delle Chiaie, an Italian far-right paramilitary man, were given the respective tasks of securing internal security and gaining international recognition. In 1980 they initiated an antidrugs campaign, which resulted in the elimination of Suárez's cocaine rivals and the suppression of other resistance to the regime. In 1981, U.S. support was rescinded, and the regime collapsed.

The economic and political developments in the 1970s, coupled with U.S. cocaine demand, drove peasants to replant coca in the Yungas region. Following the collapse of tin and Bolivian mines closing in the 1980s, many peasants migrated to the Chapare region to cultivate coca. Although the cocaine economy was marked by violence, the Chapare region farmers built their own organizational structures, the *sindicatos*, to mediate conflict, thereby creating their own forms of democracy. The coca of the Chapare region is rich in alkaloids, making it ideal for processing into cocaine rather than being chewed. The population in Chapare doubled in the 1980s. In 1987 coca was generating $3 billion per year—over one-fourth of Bolivia's gross national product.

In 1986 the United States in its war on drugs instigated Operation Blast Furnace. A force under the control of the Drug Enforcement Administration (DEA), which included six Black Hawk helicopters and two hundred personnel, attempted to stop drug trafficking in the Beni province. Resistance from local farmers halted the operation after four months, and the squad was disbanded.

The U.S.-backed Agroyungas project attempted to limit production through providing aid to farmers. The aim was to entice farmers to grow other cash crops. Villagers received improved electricity and water supplies. Initially the plan was a success, but as the farmers switched from coca to coffee, they were exposed to the vagaries of the international market. When international coffee prices dropped and fertilizer prices became prohibitive, peasants abandoned their crops. In addition, the coffee plants used in the area were susceptible to insects that devoured the coffee seeds, decimating the local coffee production. As a result, many peasants returned to coca cultivation for its guaranteed income. Other forms of crop substitution provided some initial gains but were abandoned. Lobbyists for financially strapped U.S. farmers argued that subsidies for antidrug crop substitution projects were undermining their ability to compete. The Agroyungas project was concluded in 1990.

In 1988 the Bolivian government, urged by the United States, passed the Ley 1008, which decreed

harsh penalties for drug trafficking and attempted to regulate coca production. It regulated licit supplies in the traditional Yungas region and attempted to eradicate illicit coca in the Chapare region by compensating peasants and to eradicate coca in other regions, such as Beni, without compensation. This decree resulted in the destruction of 990 acres of coca plantations in the Yungas and 790 acres in Chapare. Growers were provided with $2,000 for destroying their coca crops. Money corrupted this plan: Planters paid inspectors for a drug free certificate, poor farmers were targeted by the narcotic police who needed to meet crop eradication goals, and wealthier people bribed the police. Prisons filled with poor farmers who waited up to four years for a trial.

The issue of drug eradication foundered. There are several examples. In 1991 President Jaime Paz Zamora named Faustino Rico Toro as head of antinarcotics operations. Toro had a history of cocaine trafficking and exploited his position to solidify his cocaine operation. He was eventually exposed as a trafficker and was sentenced to Cochambamba Prison as Paz Zamora's regime collapsed with drug trafficking allegations in 1994. Cocaine cultivation declined in the later 1990s as production switched to Columbia. Bolivia tried to eliminate the drug altogether as it sought international aid.

In 1998 President Hugo Bánzer signed the *Plan Dignidad* (Dignity Plan) with the United States. This plan sought total eradication of cocaine cultivation by 2002, but it ran into serious opposition from indigenous coca growers who staged a series of protests seeking to bring down the government. The army quelled the discontent but several peasants died. The peasants then began to target the police and a surrogate war erupted.

The tensions resulted in the eventual victory of the Movimiento al Socialismo (MAS) Party, headed by Evo Morales, who was elected president in 2005. The United States brought new pressure to Bolivia to eradicate coca plantations with its emphasis on zero tolerance. The United States wanted Bolivia to implement the Dignity Plan, but the plan was perceived by the new regime as an outside imposition on Bolivian national identity. Moreover, suppression in one country entails increased production in another as the demand outstrips supply. Morales stated that he wants to preserve the legal market for coca leaves and promote the export of legal coca products. As of 2008, the government maintained that coca leaves are part of Bolivian culture, whereas cocaine should be suppressed because it is chemically manufactured and a product of the colonialists. This tolerance of coca identified Morales as opposing the U.S. zero tolerance policy.

TOBACCO

The one major Bolivian tobacco producer, Cia Industrial de Tabaco SA (Citsa), produces 12 brands, some home produced, others manufactured under license from Phillip Morris USA. This monopoly is constantly challenged by a thriving illicit market that undercuts the price through evading taxes. An estimated 50 percent of the market is contraband.

Laws passed in 2007 prohibited the sale of single cigarettes and packs of ten to curb the demand for contraband. These measures were also an attempt to set health standards and stem the high incidence of smoking among the urban poor.

ALCOHOL

The traditional alcoholic drink of Bolivia, *chicha*, is a pale sour beverage derived from corn and drunk from a gourd that has a rounded bottom so it has to be constantly held. The drinking ritual requires that a small amount of the liquid be thrown on the ground to bless the Inca goddess Pachamama, the goddess of the earth. Bolivia has its own brands of liquor, Singani, which is made from grapes and usually combined with a soft drink mixer to make a chuflay. It also produces its own beers such as Paceña and the high-end brand Huari. Prior to the Spanish Conquest, the Incas had consumed alcohol only during religious ceremonies. Post conquest, alcohol use rose significantly as the Inca populations coped with imposed social changes that eroded their culture.

See also **Coca Plant.**

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DEAN WHITTINGTON

BORDER MANAGEMENT. The effective management of U.S. borders has become a priority for the U.S. government as it attempts to control illegal immigration, fight terrorism, and prevent the importation of illegal narcotics. Although most of the focus has been placed on the U.S.-Mexico border, increasing drug traffic and illegal immigration, coupled with national security concerns, have led to more surveillance of the U.S.-Canada border as well. The effectiveness of border management has historically been difficult because many federal agencies had some jurisdiction in this area. The failure to coordinate and consolidate border operations limited the ability of the government to meet its objectives. However, in the aftermath of the September 11, 2001, terrorist attacks on the World Trade Center and the Pentagon, the federal government has increased the funding of border management and moved agencies into the new Department of Homeland Security. In addition, public discontent over the continued influx of illegal aliens from Mexico has made border policies part of the national political debate.

ODAP REVIEW AND RECOMMENDATIONS

In 1977, a U.S. government interagency team led by the Office of Drug Abuse Policy (ODAP) conducted a comprehensive review of border control and recommended consolidation of the principal border control functions into a single border management agency. Executive departments failed to agree on distribution of resources and organizational placement of the new agency, however, and so the border management agency never materialized.

Border control in the United States was described in the ODAP review as an extremely complex problem involving vast distances, many modes of transportation, millions of arrivals and departures, and millions of tons of cargo. Laws to be enforced involved illegal drugs and other contraband, terrorists, public health threats, agricultural pests and diseases, endangered species, entry visas, duties, and so forth. Nine federal agencies shared border-control responsibilities, contributing to overlap, duplication of effort, and duplicated management systems.

The ODAP report recommended consolidating the inspection and patrolling functions, including operational and administrative support. The potential for improved effectiveness in a consolidated border management agency was widely recognized. A similar report by the U.S. Government Accountability Office (GAO) also recommended single-agency management and responsibility for border control. Controversy over which activities to include and which executive department should control the new agency was, however, effective in blocking further action.

DEFINING HIDTA

The Anti-Drug Abuse Act of 1988 and the U.S. Office of National Drug Control Policy Reauthorization Act of 1998 authorized the director of the Office of National Drug Control Policy (ONDCP) to designate areas within the United States that exhibit serious drug trafficking problems and harmfully affect other areas of the nation as High Intensity Drug Trafficking Areas (HIDTA). The HIDTA Program provides additional federal resources to those areas to help eliminate or reduce drug trafficking and its harmful consequences. Law enforcement organizations within HIDTA assess drug trafficking problems and design specific initiatives to reduce or eliminate the production, manufacture, transportation, distribution, and chronic use of illegal drugs and money laundering.

When designating a new HIDTA, the ONDCP director consults with the attorney general, the secretary of the treasury, the secretary of homeland security, heads of the national drug control program agencies, and the appropriate governors. Each HIDTA is governed by its own executive board of approximately 16 members—eight federal members and eight state or local members. These boards facilitate interagency drug control efforts to eliminate or reduce drug threats. The executive boards ensure that threat-specific strategies and initiatives are developed, employed, supported, and evaluated. HIDTA-designated counties include approximately 14 percent of U.S. counties; they are present in 45 states, Puerto Rico, the U.S. Virgin Islands, and the District of Columbia. The Southwest Border HIDTA (California, Arizona, New Mexico, and Texas) was established in 1990. It is subdivided into five regions, encompassing 47 counties in the four Southwest border states.

CONGRESS PASSES IIRIRA

Major change came when Congress passed the Illegal Immigration Reform and Immigrant Responsibility

Act of 1996 (IIRIRA). The IIRIRA is a tough, enforcement-oriented law that seeks to restrict the passage of undocumented aliens across the U.S. borders. The IIRIRA mandated increasing the number of U.S. Border Patrol agents by 5,000. The law also mandated that the additional Border Patrol agents be deployed in sectors along the border in proportion to the number of illegal crossings at each sector. The legislation, however, requires that the attorney general coordinate with and act in conjunction with state and local law enforcement agencies to ensure that deployment of resources to the border does not degrade or compromise the capabilities of interior Border Patrol stations.

Even before the passage of the IIRIRA, the Border Patrol had begun to implement new enforcement strategies. A 1998 GAO report noted that the Immigration and Naturalization Service (INS) had made progress in implementing some, but not all, aspects of the necessary strategy to curtail illegal entry in the Southwest. The strategy, begun in 1994, called for the Border Patrol to (1) allocate additional resources in a four-phased approach, starting with the areas of highest-known illegal activity; (2) make maximum use of physical barriers; (3) increase the proportion of time Border Patrol agents spend on border enforcement activities; and (4) identify the appropriate mix of technology, equipment, and personnel needed for the Border Patrol. At ports of entry along the Southwest border, the strategy called for the inspection program to increase inspector staff and use additional technology to increase the deterrence and detection of illegal entry and to improve management of legal traffic and commerce.

In addition to the increases in personnel, the IIRIRA required the construction of new barriers along the border and authorized the purchase of new equipment. The law directed the attorney general to have additional barriers installed to deter illegal crossings, especially in areas of high numbers of illegal entries. The legislation mandated the construction of fencing and road improvements in the 14-mile border area near San Diego, starting at the Pacific Ocean and extending eastward. In particular, the law mandated the construction of second and third fences, in addition to the existing reinforced fence, as well as roads between the fences.

CUSTOMS AND BORDER PROTECTION ESTABLISHED

Border management became an even more pressing issue following the September 11, 2001, terrorist attacks. In 2003 Congress established the Department of Homeland Security, which contains federal agencies once housed in other departments. U.S. Customs and Border Protection (CBP) is an agency that is charged with regulating and facilitating international trade, collecting import duties, and enforcing U.S. trade laws. Its other primary mission is to prevent terrorists and terrorist weapons from entering the United States. CBP is also responsible for apprehending individuals attempting to enter the United States illegally and for stemming the flow of illegal drugs and other contraband. Former agencies subsumed under CBP include the U.S. Customs Service, the Border Patrol, and the Immigration and Naturalization Service. The Office of Intelligence and Operations Coordination (OIOC) is a new agency that coordinates antiterrorism efforts.

One of CBP's major efforts in curtailing illegal immigration and the importation of illegal narcotics is the Secure Borders Initiative, popularly known as SBInet. SBInet is an attempt at an integrated solution for border management, using the best mix of personnel, infrastructure, and technology to detect and respond to breaches of the borders with Mexico and Canada. What makes this initiative different from past efforts is the hiring of a private corporation (Boeing) to develop the suite of technological tools that CBP will use to coordinate border security. The goal of SBInet is to cover the entire 6,000 miles of international border; its first stage is 28 miles in the Tucson, Arizona, sector. This sector is the most heavily trafficked area of the border, making the pilot project a good test for the new system. The pilot project will examine the usefulness and reliability of technology that may include sensors, thermal imagery, remote cameras, and improved communications. Infrastructure changes may include roads, bridges, fences, and improved lighting. Under SBInet, Boeing is required to provide a solution that not only advises an agency of an entry but also identifies the entry, classifies the entry as to threat, supplies a means to efficiently respond to an entry, and brings the entry to the appropriate law enforcement agency for resolution.

Despite efforts such as SBInet, border management under the CBP has continued to draw criticism. A 2007 report by the GAO estimated that 21,000 people who should not have been allowed to enter the U.S. came through official border crossing points between October 1, 2005, and September 30, 2006. Staffing problems and poor management were cited as reasons that persons were able to enter the country improperly. Another 2007 GAO report also found that the terrorist watch list was not being used consistently throughout the border management system.

As for policing illegal narcotic shipments, CBP has employed technology to assist its agents. For example, giant X-ray machines have been installed at ports of entry. Trucks and their cargo are examined in this unobtrusive way to detect cocaine vapors. Other high-tech equipment, such as night-vision goggles, motion sensors, and low-light TV cameras, are now being used on the border.

See also **Drug Interdiction; Operation Intercept; U.S. Government Agencies: U.S. Customs and Border Protection (CBP).**

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BRAIN STRUCTURES AND DRUGS.

Psychoactive or behaviorally active drugs are substances that alter internal and external behavioral processes, including activity levels, emotions, and cognitive ability. As a result of these effects, using some of these substances can lead to compulsive drug use and drug addiction, while using others can manage neuropsychological disorders. In both cases these drugs modify existing neuronal systems and their function. To understand the actions of drugs on the brain, it is necessary to understand the molecules that these drugs interact with and how these interactions affect the brain circuits and systems that regulate normal, adaptive behavior. This entry contains information intended to assist readers in understanding the biological basis of drug actions on the brain and particularly the actions of commonly abused drugs. First, the general classification of brain cells is discussed and then brain structures and circuits as they relate to normal, adaptive function and drug action. The classification of brain cells based on the chemical nature of communication between cells is then discussed as it relates to the actions of abused drugs.

CLASSIFICATION OF BRAIN CELLS

The brain is a complex structure that has many different types of cells. Brain cells are subdivided into two general categories based on a number of criteria, including (1) neurons (nerve cells) that rapidly (in the space of milliseconds) receive and transmit information through specialized structures termed synapses (points of communication between neurons containing specialized structures to release, receive, and eliminate neurotransmitters), or (2) glia, which maintain a homeostatic, balanced environment that allows for efficient communication between neurons. Neurons are further subdivided according to (a) shape or size; (b) their connections; (c) the distance over which they transmit information; and (d) which chemicals are released to transmit information to other cells. Although a role for glia is becoming more appreciated, most of the effects produced by psychoactive drugs that are well understood result from actions on neurons that process or transmit information through synapses. However, in general, actions of drugs on the brain are complex and seldom involve only one type of brain cell. Neurons in one brain region send inputs to and receive outputs from

other regions. These factors have made the identification of specific cells in the brain responsible for a given drug effect difficult to distinguish. This fact applies even to the simplest behaviors, which involve complex interactions among millions of cells. For these reasons, the understanding of the processes underlying addiction is incomplete; however, as explained below, significant progress was made in this area between 1985 and the early twenty-first century.

ORGANIZATION OF THE BRAIN: BRAIN REGIONS

The Cerebral Cortex. A number of experimental approaches have been developed to study the neural basis of behavior. One of these approaches involved studying the role of specific brain regions in behavior. The brain is composed of distinct substructures. The most general categorization scheme separates the brain into segments called lobes. From front to back these include the frontal, parietal, and occipital lobes, and the cerebellum. The temporal lobe is on the lateral surface of the brain. The outermost surface of the brain is called the cortex; this part of the brain rapidly evolved over the last 5 million years and is responsible for the generally improved cognitive abilities found in humans relative to other organisms.

Areas of the cortex are organized in two general functions: (1) primary sensory cortex where specific information arrives through vision, audition, taste, proprioception (the unconscious perception of movement) and smell, and (2) association cortex where the primary sensory information is integrated to form a unified perception of the external world. It is the evolutionary expansion of association cortex that allows humans to create complex perceptions of the world, deduce information beyond immediate sensory experience, and to make decisions based upon this information. In particular, association in frontal cortex subserves higher cognitive functions and allows complex planning and decision making to guide adaptive behavior. Therefore, to guide adaptive behavior, the brain must integrate sensory information, emotional perceptions, and previous experiences (memories) into a predictive model of the external world and then initiate the appropriate behavioral response.

The Thalamus. Information processing includes sensory information that comes in from sense organs (e.g., eyes, ears, tongue) to the brain through the spinal cord or directly through cranial nerves (nerve cells connected directly to the brain). This incoming information from sense organs goes to a central relay station called the thalamus. The thalamus is specialized, much like the cerebral cortex, in that defined areas receive input that is specific to a sensory modality. For example, input from the eyes through the optic nerve goes to a region of the thalamus called the dorsal lateral geniculate nucleus. This area of the thalamus, in turn, sends the information transmitted from sense organs to the appropriate primary sensory area of the cortex. For example, the lateral geniculate sends visual information to the area of the cortex specialized for vision, which is located in the occipital lobe. Similarly, the cerebral cortex sends commands to the effector systems (usually muscles) that act on the environment through a parallel thalamic relay system. Obviously, the thalamus is a very important structure for the coordination of inputs and outputs from the brain. Thus, degenerative diseases of this structure are highly debilitating, as are drugs that specifically alter the function of this structure.

The Brain Stem. Other areas of the brain are responsible for life processes of which we are not usually aware. These processes are generally controlled by the part of the brain called the brain stem, which is located between the spinal cord and the cerebral hemispheres of the brain. The brain stem is evolutionarily the most primitive portion of the brain and contains the cell bodies that maintain critical life functions, such as heart rate, blood pressure, breathing, and other involuntary or unconscious life-sustaining processes. A number of psychoactive agents have actions on neurons located in the brain stem. For example, opiates such as morphine or heroin have a direct inhibitory effect on the brain stem respiration (breathing) centers, which explains why heroin overdoses are often fatal—the breathing centers stop working. A significant part of the reticular formation is also located in the brain stem. This system sends outputs into the brain and down the spinal cord. It regulates arousal by increasing or decreasing the brain's responses to environmental events. The brain stem is also important in the control of pain

and contains the cell bodies for some important nerve cells involved in the euphoric (pleasurable) and depressant actions of drugs.

BRAIN SYSTEMS

The Limbic System. Another important anatomical brain system through which abused drugs act is the limbic system. This system is a collection of structures that lie between the brain stem and the cerebral cortex. It includes the olfactory bulb, prefrontal and cingulate cortices, nucleus accumbens, amygdala, hypothalamus, hippocampus and septum, all of which have direct connections with one another. Parts of the brain stem are also included in the limbic system because of their strong connections to the other brain regions in the limbic system. In particular, the dopamine cells in the ventral tegmental area send strong projections to the rest of the limbic system. The limbic system is involved in the control of motivated behaviors, such as eating, drinking, and sexual behaviors, and in the expression of emotional behaviors, including anxiety and aggression. Tumors or lesions of these structures often lead to abnormal emotional expression. Drugs that directly affect this system can produce changes in goal-directed behaviors, mood (euphoria-dysphoria), and emotions. Importantly, drugs of abuse directly or indirectly modulate the dopamine projections within the limbic system to reinforce drug-seeking behavior.

The Motor System. Motor function (movement) involves a number of brain structures that include the caudate nucleus-putamen, which sits above and in front of the thalamus, the premotor cortex, and the motor cortex as previously described. This system is particularly important in generating repetitive behaviors, such as those involved in the conduct of daily tasks that are habitual (such as riding a bike or typing a letter). The fact that the use of addictive drugs becomes habitual is thought to strongly involve the habit circuitry in motor systems.

NEUROTRANSMITTER SUBSTANCES

Besides categorizing the parts of the brain by structure, the brain can also be separated into systems based on the distribution of the chemicals that nerve cells use to communicate with one another. Thus, cell bodies for some important nerve cells are localized in specific brain nuclei (collections of nerve cell bodies). Some drugs of abuse have specific actions on subsets of cells that use or release a specific chemical to communicate with other cells. For example, alcohol (ethanol) is believed to act on at least four systems in the brain: the ones containing the nerve cells that release dopamine, serotonin, glutamate, and gamma-aminobutyric acid (GABA). The cell bodies of dopamine- and serotonin-releasing nerve cells are localized to specific brain stem regions and project widely to the limbic system, while glutamate-releasing and GABA-releasing cells are distributed widely throughout the brain.

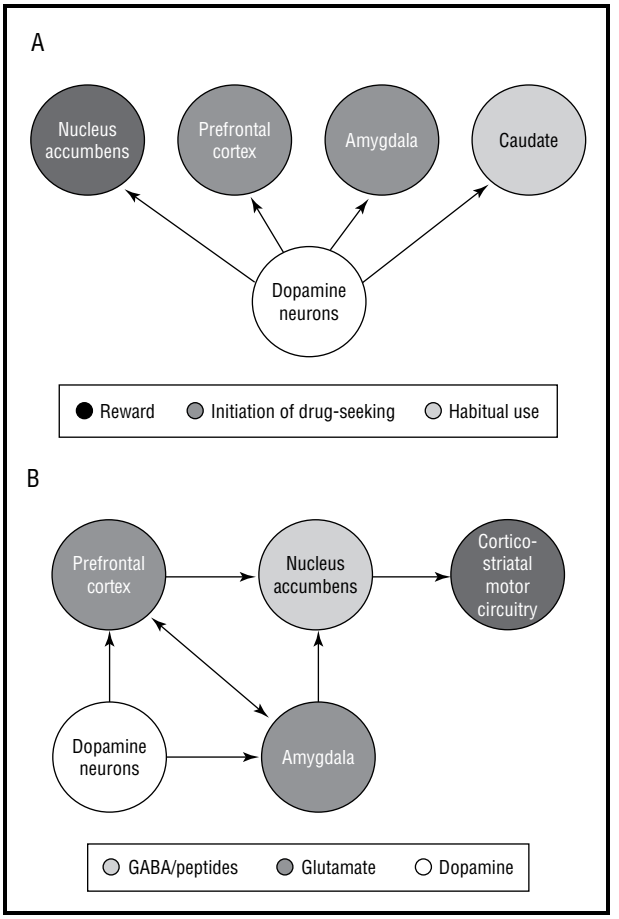

Figure 1. Neuronal circuit involved learning addictive behavior and relapse. (A) The major components of the system for learning drug-seeking behaviors are the same as learning normal reward seeking, and include the dopamine pathways from the ventral tegmental area to the nucleus accumbens caudate, amygdala, and frontal cortex. The role of these regions in reward learning can be simplified as indicated in the legend. (B) The circuitry underlying relapse involves the same structures involved in learning and is precipitated by dopamine release into or sensory activation of the prefrontal cortex and amygdala followed by involvement of the nucleus accumbens and caudate (corticostriatal) habit pathways. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Readers may wonder where the different actions of drugs of abuse occur in the brain. The simple answer is that drugs act directly or indirectly on dopamine neurons to increase dopamine release into the limbic system. Thus, while the drug itself may not directly affect dopamine release, through actions on nerve cells adjacent to the dopamine system, the drug does release dopamine. Next is a brief description of how different classes of drugs of abuse act to release dopamine. Stimulant drugs (e.g., amphetamine, cocaine, methamphetamine) produce overall effects on the brain resulting in increased activity, faster speech and thought patterns, and euphoria. This overall effect results from an ability to increase brain dopamine levels by preventing the elimination of dopamine from the brain. Alcohol is thought to activate dopamine systems by inhibiting the GABA neurons that normally inhibit dopamine cells, thereby releasing the dopamine system from inhibitory control. Nicotine also stimulates dopamine cells, in part by acting directly on dopamine cells and in part by releasing glutamate onto dopamine cells to indirectly excite them. Opioids (e.g., heroin, morphine, oxycodone) do not act directly on dopamine cells, but on the GABA neurons regulating dopamine cells. Thus, by inhibiting GABA cells, the opioids activate the dopamine cells.

BIOLOGICAL BASIS OF ADDICTION

Activation of Reward Learning. The capacity to learn behavioral strategies to obtain rewarding stimuli such as food and sex is central to human survival and adaptation to the environment. The brain circuitry mediating this essential function is outlined in Figure 1 and shows that the mesocorticolimbic dopamine system is a central component of it (Berridge & Robinson, 1998). A common effect of all drugs of abuse is to stimulate reward learning by activating dopamine transmission. New rewarding situations stimulate dopamine release to facilitate the development of behaviors designed to obtain the reward. Addictive drugs pharmacologically stimulate dopamine release, thereby mimicking this reward learning neurochemical situation and promoting the development of behaviors to obtain the drug in the future. This process is often called the reinforcement of behavior, and most addictive drugs release far more dopamine than can be physiologically achieved by natural rewarding stimuli. Accordingly, addictive drugs strongly reinforce drug-seeking behavioral strategies, ultimately to the exclusion or diminution of behavioral strategies designed to obtain natural rewards, such as friendship, social cooperation, and even food and sex. Indeed, well-learned drug-seeking strategies become largely unconscious and proceed as a procedural memory, akin to riding a bike, where once the task is well learned the bicyclist no longer consciously thinks about how to ride the bike (Kelley, 2004).

Addiction as a Compulsive Drug-Seeking Behavior. Once drug-seeking behaviors are well learned, the release of dopamine is not required for an addict to seek the drug and relapse to using it. Rather, as a learned behavior, the motivation to obtain the drug relies predominantly on cortical and allocortical drive into motor circuits in the brain, including the nucleus accumbens and caudate. Thus, as shown in Figure 1, brain areas such as the prefrontal cortex, amygdala, and hippocampus send glutamatergic projections into the basal ganglia motor circuit. In particular, glutamatergic projections to the nucleus accumbens are thought to be strongly modified by chronic drug use, making it increasingly difficult for an addict to control his or her behavior and making the addict increasingly vulnerable to relapse. Using animal models, some studies have catalogued many enduring changes in these projections that are associated with chronic drug use and contribute to relapse vulnerability (Kalivas & O'Brien, 2008). This includes molecular changes that result in poor regulation of glutamate release and changes in how the neurons interpret both glutamate and dopamine signals. This loss of synaptic homeostasis parallels the loss of behavioral homeostasis that characterizes addiction (Koob & Le Moal, 2001). Importantly, the loss of homeostasis, or allostasis, is progressive and typically worsens as more of the drug is used. A goal of research in this area in the early twenty-first century is to identify the molecular changes produced by chronic drug use and to reverse them in order to restore synaptic homeostasis and thereby permit an addict to achieve greater control over the motivation to seek the drug and relapse to using it.

Addiction as a Disease of Adolescence. The vast majority of drug addicts begin drug use in adolescence (Volkow & Li, 2005). This fact is thought to be explained by the neurobiological

development of the brain that takes place during adolescence. The adolescent brain has a larger number of synapses in the prefrontal cortex than the brain of an adult. Likewise, dopamine concentrations are elevated in adolescence. Thus, normal adolescent brain development involves the gradual pruning back of synapses in the prefrontal cortex. The greater number of synapses and dopamine content is thought to contribute to the high level of exploratory behavior and risk taking in adolescents as compared to adults. This exploratory activity has obvious evolutionary advantages by allowing adolescents to discover and interpret their environment in order to develop the adaptive, enduring behavior patterns that increase the probability of becoming stable and nurturing adults. Thus, the capacity of the environment to influence and change an adolescent is much greater than for an adult, and the repeated exposure to addictive drugs has a more profound shaping influence on the adolescent brain. Included in this shaping is the reward learning of behaviors that maximize obtaining drug reward, making the adolescent particularly prone to developing addictive behaviors.

USING NEUROBIOLOGY TO TREAT ADDICTION

This is a simplified description of complex neuronal networks that are believed to play a major role in the development of drug addiction as a compulsive relapsing disorder. In some ways knowledge is fairly complete, such as to which molecules a drug binds in the brain, but knowledge of how this initial drug action changes behavior and comes to dominate a person's life is as of 2008 yet to be clarified. The key to this understanding is the emerging knowledge of how the brain works both in terms of its circuitry and at the molecular level to interpret the world as context and to establish new behaviors. Addictive drugs usurp this process and produce pathological changes in this brain machinery. Reversing these changes promises to determine the future in treating and ultimately curing addictive disorders. To accomplish this goal, pharmacological therapies need to be coupled with psychosocial interventions. Pharmacologically restoring normal brain functions can permit the resolution of addiction, but psychosocial interventions are necessary to help addicts rebuild their lives.

See also **Alcohol: Chemistry and Pharmacology; Dopamine; Neurotransmitters; Opiates/Opioids; Overdose, Drug (OD).**

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BREATHALYZER. Breath-analysis machines detect and measure the alcohol present in deep lung air and convert this to an estimate of blood alcohol concentration (BAC). This calculation is based on the small but constant proportion of alcohol that the body excretes through the lungs. Regardless of interpersonal variations in metabolism, for legal purposes in most countries, the BAC is a ratio of breath to blood of 1:2100, although research indicates that the ratio of 1:2400 is more accurate (Swift, 2003). Breath analysis machines use methods such as thermal conductivity and infrared absorption to detect alcohol in lung air. Because breath alcohol analysis is quick and non-invasive, it is a useful tool in a variety of situations. The breathalyzer has traditionally been associated with law enforcement agencies for monitoring drinking and driving. However, it is increasingly being used in clinical settings. A number of models—both portable and fixed ones—are available.

Breathalyzer is the trade name of the model manufactured by Smith and Wesson, but the name

has become synonymous with breath test machines. Breath-analysis machines have emerged as a powerful tool for law enforcement officers in policing motorists who may be operating motor vehicles while under the influence of illegal levels of alcohol.

Officers routinely conduct field sobriety tests on motorists they suspect of driving while intoxicated. An officer first requests that the motorist suspected of intoxication perform certain physical tests, such as walking a straight line, putting a finger to the nose, or balancing on one foot, in order to corroborate the officer's suspicion of intoxication of the motorist based on objective findings. If the officer concludes that the motorist has failed one or more of these tests, the officer requests that the motorist submit to a breathalyzer test. The results of the test either bolster innocence or corroborate police opinion testimony of intoxication, or in those states that set presumptive blood alcohol intoxication levels, to demonstrate that the motorist's blood alcohol level exceeded the permissible level.

If a motorist refuses to take a breathalyzer test, the police cannot compel the person to take the test. However, states have enacted implied consent laws that are civil, rather than criminal, in nature. Under these laws, if a motorist refuses to take the breathalyzer test, the motorist's driver's license is automatically suspended for a set period of time. Thus, motorists who are confronted with the alternatives must balance the criminal sanctions that follow a high alcohol reading from the breathalyzer against the immediate suspension of their driving privileges. However, in the late 1990s, some states, including New York and California, enacted laws that made refusing a breathalyzer test a crime. In these and several other states, legislators concluded that a license suspension was not a severe enough penalty for drunk drivers.

Because breathalyzer test results serve as powerful incriminating evidence, defendants and their lawyers often seek to challenge the reliability of the tests. This has produced a group of experts that routinely testify as to the way the test was administered and the reliability of the breathalyzer machine itself. The breathalyzer must be calibrated periodically. Calibration is a procedure performed by laboratory personnel to ensure the accuracy and reliability of the instrument. Routine maintenance is also performed to ensure the continued accuracy and proper function of the breathalyzer. Once calibrated, a certificate of calibration is completed by the laboratory and a certified copy provided to the law enforcement agency using that breathalyzer. Failure to follow maintenance schedules can raise a reasonable doubt about the machine's results and lead to an acquittal. Apart from the alleged technical defects of a breathalyzer, experts often testify that the officer failed to follow the proper protocol for operating the machine or that the defendant's blood alcohol level was incorrectly inflated due to biological factors.

Breathalyzers are also being used as preventive devices. In some states, courts order persons convicted of repeat offenses for driving while under the influence of alcohol, to install a breathalyzer interlock on their cars. The driver must breathe into the machine before starting the car. If the alcohol level is too high, the car will not start. After the car has started, the driver must periodically breathe into the device for a retest. If the driver fails the test, the car honks its horn and flashes its lights. Safety measures have also been developed to prevent circumvention of the protective device by using special driver recognition methods to prevent an unauthorized person from giving a breath sample.

Disposable home alcohol breathalyzer tests are widely available and come in handy to do a quick test. The test consists of a disposable tube that contains yellow crystals, which turn green in the presence of alcohol. As breath passes through the tube, the length of the green color change indicates whether one is above or below the legal driving limit. Any green color change indicates the presence of alcohol in a person's breath. The product is not to be used in a court of law. Additionally, the manufacturer, suppliers, agents, distributors, and retailers assume no responsibility for consequences when persons who test negative with this device are later discovered to be under the influence of alcohol or to have their judgment impaired by alcohol.

See also **Driving Under the Influence (DUI).**

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BRITAIN. The legal use of what are now termed *illicit drugs* was widespread in 19th-century Britain. Opiates in various forms were used at all levels of society, both for self-medication and for what is now called "recreational use." At that time, the differentiation between medical and nonmedical usage was not clearly established, and concepts such as "addiction" were not widely accepted. The story of drug use in Britain since the late 19th century is the story of how and why drugs came to be defined as a social problem. A number of factors led to the establishment of certain forms of drug-control policy although they often had little relationship to the objective dangers of the drugs concerned.

EARLY EFFORTS AT CONTROL

In the early 20th century, there was limited involvement by either doctors or the state in the control of drug use and addiction. The supply of opiates and other drugs in Britain was controlled by the pharmaceutical chemist. As dispensers and sellers of drugs over the counter, they were the de facto agents of control. A rudimentary medical system of treatment operated via the Inebriates Acts (codified in the 1890s), whereby some inebriates could be committed to a form of compulsory institutional treatment. Legislation covered only liquids that were drunk (e.g., laudanum), and not injectables. Users of hypodermic morphine or cocaine were therefore not included under this system.

Drug addiction was not perceived as a pressing social problem in early 20th-century Britain, nor, indeed, was it one. During this period, the number of addicts decreased and overall consumption declined. No specific figures are available, but various indicators, such as poisoning mortality statistics, confirm this conclusion. Nevertheless, the 20th century brought increased controls and the classification of opiates and other drugs as "dangerous." Drugs classified in this way were regulated through a penal system of control rather than through the mechanisms of health policy.

Two factors brought about regulation. The first was Britain's involvement in an international system of drug control; the second was the impact of World War I (1914–1918) and its aftermath. U.S. pressure on the international scene pushed an initially unwilling Britain into a system of control that rapidly expanded from the regulations discussed at the 1909 Shanghai Convention to the worldwide system envisaged at the Hague Opium Convention of 1911–1912.

Prior to World War I, however, only the United States, by way of the Harrison Narcotics Act of 1914, had put this system of drug control into operation. Britain favored a simple extension of the existing Pharmacy Acts. The influence of emergency wartime conditions, however, brought a differently located and more stringent form of control. The fear of a cocaine epidemic among British soldiers patronizing prostitutes in the West End of London—a fear that, on later investigation, proved to have been largely illusory—allowed the passage of drug regulations in 1916 under the Defence of the Realm Act. International drug control, in turn, became part of the postwar peace settlement at Versailles. The 1920 Dangerous Drugs Act therefore enshrined a primarily penal approach, and drug control was located in the Home Office rather than in the Ministry of Health, which was established in 1919.

TWO APPROACHES

British drug policy was henceforward marked by a tension between rival conceptualizations of the drug-addiction issue—drugs as a penal issue versus drugs as a health matter. The 1920s saw this conflict at its height. Britain seemed likely to follow a penal course similar to that of the United States, and British legislation was consciously modeled on the Harrison Narcotics Act. British doctors soon reasserted their professional control, however. In 1926, Britain's Rolleston Report legitimated a medical approach that could entail medical "maintenance prescribing" of opiates to a patient who would otherwise be unable to function. The Rolleston Report established what became known as the British System of drug control. This was a liberal, medically based

system, albeit one that operated under Home Office control.

This system remained in operation for nearly forty years, until the rapid changes of the 1960s forced a reassessment. During the 1920s, 1930s, and 1940s, the number of addicts were small and there were few nonmedical users (less than 500). It is generally recognized that the British System of medical control operated because of this situation, rather than as the cause of it. This equilibrium began to break down after World War II (1939–1945), when a more extensive recreational, or nonmedical, use of drugs (such as heroin and cocaine) began to spread. There were a variety of reasons for this spread, including the spread of cannabis (marijuana) from the new immigrant population to the white population, the overprescribing of heroin by a number of London doctors, thefts from pharmacies, and the arrival of Canadian heroin addicts. Other drugs, particularly amphetamines, also became recreationally popular.

A GROWING PROBLEM

The official number of heroin addicts rose rapidly—from 94 persons in 1960 to 175 in 1962. The number of cocaine users, meanwhile, increased from 30 in 1959 to 211 in 1964. Nearly all of these were nonmedical consumers. The average age of new addicts also dropped sharply. Initial government reaction, in the 1961 report of the first Brain Committee, was muted. The second report, however, which came out in 1965 after the committee had been hastily reconvened, had an air of urgency. Controls were introduced on amphetamines in 1964. The report's proposals (implemented in the Dangerous Drugs Act of 1967) took the prescribing of heroin and cocaine out of the hands of general practitioners and placed it in those of specialist hospital doctors working in drug-dependence units. A formal system was established that notified the Home Office about addicts.

The clinic system established in 1968 did not operate as originally intended. In the 1970s, as the rise in the number of addicts appeared to stabilize, clinic doctors moved toward a more active concept of treatment, substituting orally administered methadone for injected heroin, and often insisting on short-term treatment contracts rather than on maintenance prescribing. These clinic policies aided the emergence of a black market for drugs in Britain in the late 1970s. An influx of Iranian refugees from the Islamic Revolution of 1979, who brought financial assets in the form of heroin, also stimulated the market.

The British elections of 1979 returned a Conservative government with a renewed emphasis on a penal response to illicit drugs. Britain participated enthusiastically in the U.S.-led international "War on Drugs," but there were also strong forces inside Britain arguing for a more health-focused approach. In 1985 the discovery of acquired immunodeficiency syndrome (AIDS) among injecting drug users in Edinburgh, Scotland, was the trigger for policies that emphasized the reduction of harm from drug use rather than a prohibitionist approach. Nevertheless, in the early 1990s the tension between penal and health concepts and the interdependence of the two approaches to policy still remained unresolved.

THE PROBLEM WORSENS

The use of drugs within British society continued to expand in the 1990s and 2000s. Amphetamines are still second only to cannabis as the most widely used drugs in the United Kingdom, but few users are in contact with drug treatment services or seek any medical help. Services are oriented toward opiate users, and black-market amphetamine is not expensive, so there is a lower likelihood that financial problems will force users into treatment. Heroin use has also increased. During the 1980s this growth emerged in a large number of communities around the country, and it did so in a pattern different from that of the 1960s. This new pattern of use mainly involved adolescents and young adults, and the heroin was taken by a new method called "chasing the dragon"—a process in which the heroin is heated on tin foil, with the vapors being inhaled through a tube. But there was great regional variation, with injecting still popular in some areas. Overall, however, heroin use continued to grow: the number of known addicts rose from about 5,000 in 1980 to approximately 50,000 in the late 1990s, and by the mid-2000s it easily exceeded 100,000.

Cocaine use has also increased. In 1996, just over 1 percent of the population from 16 to 24 years of age reported ever having used cocaine. By

2003–2004, however, almost 5 percent of this age group reported cocaine use. Yet the speed and penetration of crack cocaine into the country has not been as rapid or as substantial as U.S. commentators had predicted. In the early 2000s only a fraction of a percent of persons 16 to 59 years of age told researchers that they had used crack. Indeed, in 2003–2004, heroin was still identified as the main problem drug for two-thirds of individuals entering drug treatment. The use of Ecstasy (MDMA, or methylenedioxymethamphetamine) received wide media publicity during the late 1990s and early 2000s, but surveys suggest it is used less frequently than other "dance drugs" such as amphetamine. The use of hallucinogens such as LSD has decreased considerably, although, in contrast, psilocybin, or "magic," mushrooms have become more popular.

NATIONAL STRATEGIES

For most of the 1990s, the British government has continued to publish national strategies on drugs, the first of which appeared in the 1980s. In 1995, *Tackling Drugs Together: A Strategy for England, 1995–1998* was published, and strategies for Scotland and Wales followed. The strategy committed the government to take effective action through law enforcement, accessible treatment, and a new emphasis on education and prevention to increase community safety and reduce drug-related crime. The strategy also attempted to reduce both young people's drug use and the health risks and damage associated with drug use. In 1998 the new Labour government published *Tackling Drugs Together to Build a Better Britain: The Government's Ten Year Strategy for Tackling Drug Misuse*, which reiterated these main themes. That same year, a former chief constable, Keith Hellawell, was appointed "drug czar," or national coordinator; his deputy had a background in rehabilitation services. Hellawell resigned in 2002, partly in protest over the reclassification of cannabis as a Class C drug, and he was not replaced.

In the 2000s, the relationship between penal and health responses in drug policy has remained central. A series of interventions have been developed that are designed to get drug users out of crime and into treatment. These include arrest referral schemes and drug treatment and testing orders, which provide an alternative to custody for drug-using offenders who agree to undergo treatment. A drug court system, similar to those in the United States, is being piloted in London and Leeds. At the same time, treatment services in prisons have expanded since the incorporation of the prison health service into the National Health Service, and new treatment programs and a through-care service for drug-using prisoners have been set up. However, mandatory urine testing in prisons and the testing of individuals for drugs upon arrest, rather than after being charged with an offense, have proved controversial.

Some policy analysts have argued that U.K. policy is moving to a harsher stance—in effect, toward coercive or compulsory treatment, with a greater emphasis on criminal justice initiatives. Despite this, there have been a series of other developments that continue to emphasize the health aspects of drug use. In 2001 the government established the National Treatment Agency (NTA), which has a remit to improve the availability and effectiveness of drug treatment services. Drug treatment, and particularly methadone maintenance, is regarded as a way of reducing drug-related crime. The new criminal justice measures on drugs have also brought more drug users into treatment instead of sending them to prison. Thus, the duality of policy approaches clearly continues.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Britain: Alcohol Use and Policy; Britain: Tobacco Use and Policy; Canada, Drug and Alcohol Use in; China; Eastern Europe; France; Germany; International Control Policies; Ireland, Republic of; Italy; Netherlands; Opiates/Opioids; Opioid Dependence: Course of the Disorder Over Time; Opium: International Overview; South Africa; Treatment.**

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BRITAIN: ALCOHOL USE AND POLICY.

The place of alcohol in British society, and the state's policy toward it, have long been hotly contested topics. Images and perceptions of alcohol in Britain have varied dramatically from one generation to another and the discourse relating to alcohol has been constantly shifting. Through the nineteenth and twentieth centuries, alcohol control was debated and shaped successively in terms of the free market (1820–1830s), of moralistic individual behavior (1840s–1860s), of social reform (1870s–1914), of national efficiency (First World War) of leisure (1920s–1930s), of health (1950s–1980s), of competition policy (1990s), and as a public order issue (early 2000s). In the early twenty-first century official attitudes toward alcohol are complex, with government agencies or departments having various attitudes. On the one hand, there are worries about health implications of excess consumption and issues of late night disturbances, but at the same time there have been moves to liberalize sales of alcohol in the interests of promoting tourism and the booming British *night time economy*.

PATTERNS OF CONSUMPTION

One characteristic of British consumption has been the propensity, alongside normal drinking, for sections of the community to indulge in periodic bouts of excessive alcohol consumption. The excesses of the *gin age* in the eighteenth century, the weekend drinking of Victorian industrial workers to the detriment of Monday work performance, the excesses of the highly paid shipyard and munitions workers of World War I, and the early 2000s *binge drinking* by young people in town centers and entertainment spots are all examples of this.

In the preindustrial age alcohol use and customs pervaded all areas of social life, with beer and spirits the preferred beverages, although whisky was dominant in Scotland. The inns and alehouses were indeed centers of community life and varied greatly in character. However, from 1850, the range of social activities carried out in the public house began to contract and the *pub* became more a leisure center for the working class, with the middling and upper social groups preferring to drink at home or in clubs, although public houses and off licenses also catered for a flourishing trade in alcohol fetched from the bar and consumed at home. Pubs came in all sorts and sizes, ranging from old inns, to city gin palaces, to sleepy rural establishments to decrepit and unsanitary beer houses. By the end of the nineteenth century the vast majority of pubs were owned by regional or national brewers on a tied house system, which strictly limited the range of beverages available to the consumer.

Per capita consumption of alcohol steadily dropped from its peak in the 1880s and 1890s to a trough in the 1950s. Large numbers of smaller and less salubrious pubs were swept away, and the larger brewers pursued a policy of providing larger improved houses with far more comfortable and better leisure facilities. These appealed to the middle classes and to women drinkers. The period from 1980 into the early 2000s, however, saw a dramatic shift in British drinking habits. The alcoholic beverages industry came to be dominated by large multinational companies, and the pubs largely owned by leisure companies rather than brewers. The number of pubs sharply declined, with those that remained specializing in themes and in providing catering and entertainment. The drinks industry set out to appeal to the youth market by advertising and promoting exotic drinks, especially those with fruit flavors or served with mixers. There was also something of a feminization of alcohol, again promoted by advertising, and rates of female drinking among the young rivalled those of men. There was a marked shift in consumption patterns. Beer sales, especially traditional ales, declined, in contrast to spirits and to wine. Although sales in public houses declined, there was a shift in sales to supermarkets and off licenses. The price of alcohol, particularly of wine, fell significantly after the 1960s in real terms, under the influence of competition regulations from the European Union. The result was a sharp rise in per capita consumption levels, back to those of a hundred years earlier; alcohol became more embedded in the leisure culture, entertainment industries, and social mores, appealing across the generations.

REGULATION OF ALCOHOL SALES

Governments in Britain were concerned about the dangers of intoxicants as far back as Tudor and Stuart times, largely on account of their potential for stirring up sedition or criminality. Accordingly, alcohol came to only be sold with an excise license and with permission from the local justices of the peace. The Home Office was the government department that had overall responsibility for licensing and alcohol issues. Although a free trade in beer in special beerhouses was allowed between 1830 and 1869, the Victorians systematized and tightened the licensing laws. However, this control and regulation was minimal and in no sense expressed a policy of promoting temperance. Although after 1860 elite politicians became concerned about the social evils of drinking, they were wary about regulating for the working class in advance of public opinion.

Restrictions on Sunday hours of sale were the only notable exceptions. Inspired by U.S. examples, many people in the temperance movement argued passionately for the local veto, a device whereby local communities could vote to be drink free. However, they showed scant interest in building coalitions for more general reform of liquor licensing, for example, schemes for a broader local control by elected boards or councils as part of local government reform, even though there was considerable support for such local solutions among politicians. Another problem was the way in which the drink issue became polarized in party political terms with the majority of the drink *trade* (businesses) throwing its weight behind the Conservative Party and the prohibitionists supporting the radical wing of the Liberal Party, making the building of consensus difficult.

The First World War saw something of a moral panic about the supposedly adverse effects of alcohol upon the war effort, and a Central Control Board was set up to impose restrictions and in some limited areas run the whole trade itself along disinterested management lines. The Board set about a positive program of improving pubs and encouraging catering and counterattractions. The Board itself was abolished soon after the war, but its legacy lived on in the form of higher taxation on alcohol, as well as restricted opening hours of public houses. Late-night opening was prohibited and an *afternoon gap* introduced, which remained a feature of British alcohol laws for the next fifty years. Eighteen was settled as the minimum age when alcohol might be purchased. During the mid-twentieth century the political salience of the alcohol issue declined, and the issue was less polarized between political parties. The drinks industry henceforth astutely developed a network of lobbyists in Whitehall, the seat of executive power.

The period between 1970 and the early 2000s was characterized by policies of marked liberalization of sales. This pattern in part reflects the libertarian political culture of modern Britain, the importance of tourism in the economy, the impact of the European Union, and the extent to which alcohol has become entwined with the broader leisure industries. Liberalization took the following forms: a) widespread sales from supermarkets with minimum restrictions on hours of sale and accompanied by promotional offers; b) efforts to ensure free competition and the play of market forces; and c) an effective end to restrictions upon the hours of sale. The afternoon gap was abolished in England and Wales in 1988 (a decade earlier in Scotland) and in November 2005 a flexible pattern of evening closing was permitted, effectively allowing late-night opening. At the same time the responsibility for licensing was transferred from the local magistrates to elected local councils, although their remit and powers were very heavily constrained by guidelines from the central government.

OPPOSITION TO ALCOHOL CONSUMPTION AND ABUSE

The prevalence of cheap gin during the eighteenth century and the subsequent excesses aroused a great deal of critical attention. In this period William Hogarth (1697–1764) published many striking engravings depicting the devastating effects of cheap spirits and alcohol upon the lower classes, such as *Gin Lane* and *Beer Street.* The 1830 English Beer Act, which was an attempt to promote free trade principles and undermine monopolistic brewers in the interests of providing a purer product, also attracted an outcry on the grounds that it encouraged drunkenness and disorder. However, such criticisms tended to be episodic, and it was only after 1830 that a more organized temperance movement began to challenge the role of alcohol.

This temperance movement received strong support across the classes, particularly among

nonconformist churches and some of the major manufacturers. After 1860 prohibitionists dominated the movement up till the 1890s, but temperance sentiment of a more moderate kind flourished at the turn of the century, and elite opinion became more sympathetic seeing intemperance as a component of broader social problems.

After 1890, however, the temperance forces were weakened by internecine warfare between the orthodox prohibitionists and the supporters of Scandinavian disinterested management, a schism which lasted until the 1930s. The Society for the Study of Addiction, by contrast, provided a basis for those challenging the moralistic assumptions of the temperance movement and who saw the issue in terms of individual addiction, a medical problem. The temperance movement sharply declined in the twentieth century, and after 1945 the chief pressure on the government came from those in the medical and psychiatric professions who promoted the disease concept of alcohol. Gradually in the 1960s and 1970s the emphasis shifted toward a concern with excessive social drinking in general. Partly this change reflected shifts in medical fashion and also the increased attention paid to preventative health. In the early twenty-first century an alcohol control lobby emerged comprising policy sponsors from psychiatry, professions such as clinical psychology, social work, and sections of the medical world interested in preventative medicine, along with social care workers and joined by the remnants of the old temperance organizations and various voluntary organizations in the social field. The body, Alcohol Concern, which had an advisory function for government, provided a focus for these groupings in the 1980s and 1990s, although in subsequent years the Royal College of Physicians played a more important coordinating role.

SHIFTING APPROACHES TO ALCOHOL

In the period following 1945 alcohol policy fragmented, with a number of different government departments having their own bureaucratic viewpoint or interest. In the 1950s and 1960s the issue was predominantly seen as one of health, but no proactive policy was pursued. The liquor licensing and law and order issues remained under the control of the Home Office. The ministries of agriculture, employment and trade, and industry were stalwart supporters of liberalization and a range of pressure groups, notably the British Tourist Authority also favored this, as well as the powerful players in the drinks industry. Against this liberalization the alcohol control lobby stressed the health risks of drinking more than safe limits.

In the early 2000s, however, a good deal of media spotlight has fallen upon the antisocial effects of *binge drinking* (as used in popular parlance to denote drunken sprees) upon late-night behavior, and casualty departments of National Health Service hospitals. In 2004 the government produced an Alcohol Harm Reduction Strategy for England, stressing the gravity of alcohol problems. However, critics pointed out the lack of funding to be allocated to it and to the extent to which the strategy rested upon partnership with the drinks industry. In view of these concerns, and increasing media attention to *Britain's drink problem*, it may seem paradoxical that the government should have pressed ahead to extend drinking hours. In part the move was justified as an attempt to *civilize* drinking by encouraging a French-style café culture without the pressure of last orders at 11 p.m. closing time and the act introduced better policing and more effective local authority control. However, it also demonstrates the degree to which Tony Blair's *New Labour* government prioritized economic development and the promotion of the leisure industries. Symptomatic of this has been the shift of alcohol licensing policy from the Home Office (concerned with law and order) to the Department of Culture, Media, and Sport, whose focus is leisure activities.

The attention paid to public order issues and binge drinking has somewhat eclipsed the concern about increased levels of regular consumption among the middle-aged as a result of the fall in price in real terms. It is a paradox that the sale of alcohol between 1975 and 2005 in Britain has been subject to a liberalization of policy at a time when the reverse process has happened with smoking. Thus, although it is as of 2008 possible to find a pub to drink in at almost any hour of the day, it is illegal to smoke inside it. This situation reflects the fact that tobacco control policy has been entirely confined within a discourse of health policy (including harm to others through passive smoking), whereas with alcohol the framing of the question remains contested between health, leisure, public order, and economic spheres.

See also **Alcohol: History of Drinking (International); Britain; Britain: Tobacco Use and Policy; Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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BRITAIN: TOBACCO USE AND POLICY.

The growth of tobacco production and consumption in Britain has been dependent on developments in agriculture, the technology of production, the way that industry was organized, and the availability of safety matches. In the 19th century, tobacco was consumed through pipes or, in the case of the middle class, cigars. This usage had implications for the debate about tobacco and health.

EARLY HEALTH CONCERNS

An analysis of the *Lancet*, a British medical journal founded in 1823, indicates that, beginning about 1850, the main concerns were with the alleged links between tobacco and such general complaints as "dyspeptic derangement," insanity, paralysis, hysteria, rickets, impotence, and loss of memory. The one specific issue linked to pipe smoking was cancer of the lip. Nevertheless these concerns were never pursued systematically. Instead, tobacco continued to be linked in a random way with "muscular debility," jaundice, cancer of the tongue, "weakness of the extremities," trembling hands, and "tottering knee." In fact, one of the main concerns was over the adulteration of tobacco with substances such as sugar, alum, lime, flour, rhubarb leaves, starch, treacle, burdock leaves, endive leaves, and red and black dye.

At this time, tobacco was also seen as having health benefits. It was noted, for example, that smokers rarely suffered from tuberculosis, and its effects in alleviating stress among such groups as laborers and soldiers were well known. As early as 1872, it was reported that nicotine, cyanide, ammonia, and sulphide were constituents of tobacco smoke, and insurance companies suggested that separate mortality records should be kept of smokers and nonsmokers. Pipes began to incorporate filters at this time, and perforations were made in the bottom of the bowl, which allegedly kept the lower layer of tobacco dry and reduced the amount of oil in the smoke. Nevertheless, the principal emphasis of the *Lancet* in this period was in favor of moderation. Lung cancer was still rare, and only a minority of doctors believed that moderate smoking was harmful to adults.

It is surprising how little this debate was affected by the advent of cigarette smoking in the 1880s. It was only with the invention of the Bonsack machine in 1883—and its adoption by the W.D. and H.O. Wills tobacco manufacturer—that the mass production of cigarettes became possible. Thereafter, expenditures on advertising increased rapidly, as did consumption. Some doctors began to experiment with filters, while others warned against the practice of inhaling smoke directly into the lungs. In the same way that the growth of the tobacco industry was dependent on economic and technological trends, the development of the cigarette marks the convergence of corporate capitalism, technology, mass marketing, and advertising. However as with pipe smoking, the *Lancet* approved of smoking cigarettes in moderation, and concerns were again centered on adulteration.

In many ways, then, the stance of the *Lancet* was purity, not abolition, and its articles focused on abuse, not use. Indeed, manufacturers submitted cigarettes to the journal for medical approval. Nonetheless there were a large number of antismoking organizations, including the British Anti-Tobacco Society, the Anti-Tobacco Legion, and the Scottish Anti-Tobacco Society. In France, the Société contre l'abus du tabac (Society against the Abuse of Tobacco) was founded, also to encourage moderation and oppose smoking

among children. The *Lancet*, meanwhile, regarded these organizations as exaggerating the danger of smoking, and most of them were unsuccessful at mobilizing mass support.

Children and Smoking. The antismoking organizations founded in the early 1900s specifically to oppose smoking by children enjoyed more success. These included the British Lads Anti-Smoking Union, the International Anti-Cigarette League, and the Hygienic League and Union for the Suppression of Cigarette Smoking by Juveniles. The campaign against juvenile smoking conveys the cultural context for the relationship between smoking and health in the early 1900s. The 1904 Inter-Departmental Committee on Physical Deterioration recommended that legislation be passed to prohibit the sale of tobacco to children and its sale in sweetshops, suggestions that ultimately passed into law in the 1908 Children's Act. However, this legislation had only indirect links with the earlier anti-tobacco movements, while it had much closer connections with related debates about child labor and "national fitness."

The actual effects of smoking on the health of children were always ambiguous. More significant from the point of view of the middle-class social reformer was the way the cigarette became a badge of identity for working-class youth. Smoking was linked with the vices of adulthood—swearing, gambling, and hooliganism—and the solution that was encouraged by boys clubs was the playing of games. Most organizations that opposed smoking by children were established through churches and Sunday schools, and they had an essentially moral purpose in the context of wider debates about urbanization and physical degeneracy. Thus, opponents of juvenile smoking employed medical evidence in rather an opportunistic way, and they were essentially concerned with morality and citizenship.

SMOKING IN THE MID-20TH CENTURY

If the 19th century was the era of the pipe and the cigar, the 1950s were the heyday of the cigarette. In the 1930s, statisticians employed by insurance companies had begun to link smoking to reduced life expectancy and cancer. By the end of the Second World War, concerns about lung cancer had intensified. Changes in mortality were investigated by the epidemiologists Richard Doll and Austin Bradford Hill, whose famous article establishing the link between cigarette smoking and lung cancer was published in the *British Medical Journal* in 1950.

Nevertheless, cigarette smoking remained a widespread social activity in the 1950s, and the health dangers were only slowly communicated to the general public. Figures for Britain indicate that 64 percent of men and 37 percent of women smoked cigarettes by 1953. Criticisms of the original article by Doll and Bradford Hill were only gradually allayed by their later cohort study. In Britain, the important, and influential, first report of the Royal College of Physicians, *Smoking and Health* (1962) clarified the arguments by stating that heavy smokers were 30 times more likely to contract lung cancer than non-smokers. Sir George Godber, the nation's deputy chief medical officer, played a key role in the genesis of this report, but it also fit in with the "modernizing" agenda of the Royal College. Public health was increasingly oriented around the concept of "risk," targeting real behavior. However, real action on the ground once again followed gradually. In Britain, cigarette advertising on television was not banned until 1967, while health warnings on cigarette packets appeared in 1971.

THE GOVERNMENT RESPONSE TO HEALTH CONCERNS

The response in the 1950s and 1960s by the Ministry of Health and such bodies as the Central Council for Health Education was certainly limited. Despite the research by Doll and Bradford Hill, the Ministry of Health took little action until a report by the Medical Research Council appeared in 1957. This report declared that the link between smoking and lung cancer was one of direct cause and effect. Even so, responsibility for health education antismoking efforts was delegated to the local authorities, the most demoralized branch of the National Health Service. The posters and use of vans by the Central Council, in hindsight, appears naïve and woefully inadequate, partly because of a failure to appreciate the scale of the behavioral problem involved. Overall, scientific caution, bureaucratic inertia, commercial pressure, and anxiety about government intervention all played a part. Governments concentrated on attempting to change individual habits rather than directly controlling the industry, and the resources allocated to health education antismoking efforts were very limited. Thus, it appears that both government and the tobacco industry wanted to keep people smoking because of the wealth that cigarettes

create, with the former being made even more sensitive because of the perceived electoral implications of policy changes. In this sense, the relationship between government and industry in this area is similar to what has occurred in the food, alcohol, and pharmaceutical industries.

Politicians from the Labour Party emerge from this story with more credit than their political opponents. Despite a lack of action at the government level, Labour MPs (members of Parliament) were engaged in antismoking activities in the mid-1960s, and they were influential in the decision to ban cigarette advertising on television. Nevertheless, an examination of the ways that the health dangers of smoking were conveyed to the British public—through newspapers, radio, and television—during this period demonstrates that the way that these health messages were received were influenced in important ways by the medium through which they were conveyed. For example, while the *Guardian* newspaper reported the issues in a thorough and serious manner, the *Daily Express* argued that smokers should be allowed to make up their own minds, while the *Times* opposed government intervention. Overall, popular magazines, newspapers, advertisements, and radio broadcasts interpreted, accepted, rejected, or constructed their own views of the smoking and health controversy in fundamentally different ways.

MOUNTING EFFORTS

By the 1970s, the case against smoking had been proven and was accepted within the medical establishment, although rejected by pressure groups such as the Freedom Organisation for the Right to Enjoy Smoking Tobacco (FOREST). A second report followed from the Royal College of Physicians, *Smoking and Health Now* (1971), and this period also saw the establishment of the antismoking group Action on Smoking and Health (ASH). New developments were limited, but they were significant in two areas. The first was the recognition of the dangers of passive, or second-hand, smoking, a development that has had a significant impact on attitudes toward the risks of tobacco use. A key paper on lung cancer rates among the nonsmoking wives of heavy smokers was published in the *British Medical Journal* in 1981. Along with HIV/AIDS, this brought environmental concerns back into public health.

The second major development was the belated recognition that tobacco was an addictive substance, and that nicotine was the real cause of physical dependence.

Acknowledged in the 1960s, but not assuming policy significance until the 1990s, this increasingly called into question the idea that smoking was an essentially voluntary activity. The emphasis on addiction showed the power of pharmaceutical interests to define a new public health, in which treatment and "magic bullets" became part of the armory of prevention.

SMOKING PATTERNS

The effect of these efforts on the tobacco companies themselves was considerable, with evidence emerging from the United States that in the postwar period these companies had marketed cigarettes despite knowing full well the harmful effects of tobacco on health. At the same time, comparatively large numbers of people continued to smoke in the face of the acknowledged scientific evidence. Indeed, smoking has remained central to an individual and group identity firmly rooted in a specific liberal notion of the self. Children continue to smoke for the reasons they always have done: because cigarettes symbolize a rite of passage into an adult world. Adults, too, remain locked into a cult of individuality that opposes the standardizing tendencies of policy. In fact, there are signs of a backlash against antismoking policies, illustrating how the act of smoking continues to have a romantic status in popular culture. Nevertheless cigarette smoking is also increasingly stratified by education, social class, and ethnicity. It is also closely associated with social deprivation, and it is particularly prevalent among working-class women. Thus, the emphasis on individual responsibility runs the risk of denying that some social groups are more susceptible to behavioral risks, and of ignoring the fact that behavior is not merely a matter of choice.

Progress in some areas has been matched by delay in others. While the White Paper *Smoking Kills* (1998) noted that 120,000 people were dying each year from illnesses directly related to smoking, it was accompanied by a failure to curb cigarette advertising through motor racing. The most striking shift in tobacco use and policy in Britain has been the gradual acceptance of the argument that all workplaces and public spaces should be smoke free, which has led to the banning of smoking in pubs and

restaurants. This policy trend began in workplaces in the Republic of Ireland in March 2004, and it was subsequently introduced in Scotland (March 2007), Wales (April 2007), and finally in England (July 2007). Anecdotal evidence for Ireland indicates almost total compliance, and the picture for England is similar. Overall, smoking illustrates important trends in the focus and discourse of public health in Britain since the mid-nineteenth century.

See also **Britain; Britain: Alcohol Use and Policy; Foreign Policy and Drugs; International Drug Supply Systems; Tobacco: A History of Tobacco; Tobacco: An International Overview; Withdrawal: Nicotine (Tobacco).**

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JOHN WELSHMAN

BULIMIA NERVOSA. Bulimia nervosa is a mental disorder defined by recurrent episodes of eating unusually large quantities of food (a binge) followed by compensatory behaviors, such as vomiting, laxative abuse, and excessive exercise or fasting. Bulimia nervosa is associated with a persistent concern over body weight and shape that may include fear of gaining weight and a desperate need to lose weight. Bulimia is divided into two categories: purging type and non-purging type. Purging bulimics, who make up the vast majority of the bulimic population, use compensatory behaviors such as self-induced vomiting or inappropriate use of laxatives, whereas non-purging bulimics compensate their binges with behaviors such as excessive exercise or fasting.

Binge eating can be, and often is, triggered by environmental and psychological factors, which in turn lead to an irresistible craving for food. During a binge, a person feels out of control and consumes more calories than most people would eat in the same situation (excluding common events such as holidays or celebrations). Binges typically occur in secret and the food one rapidly consumes during a binge is typically calorie dense and nutritionally void. An episode of bingeing can result in the consumption of thousands of calories and can last anywhere from a few minutes to several hours, perhaps occurring several times a day.

EFFECTS

Binges followed by repeated use of compensatory behaviors can cause severe fluid and electrolyte imbalances. Abuse of diuretics can lead to kidney problems and severe dehydration. Purging type bulimics suffer more from these problems than the non-purging type. The electrolyte imbalances that result from these abuses can lead to seizures, cardiac arrhythmias, muscular weakness, and even sudden death. Bulimics who use purging compensatory behaviors often develop tooth decay and loss from excessive self-induced vomiting or a laxative dependency from inappropriate and prolonged usage. Furthermore, those who purge through means of self-induced vomiting can do permanent and severe damage to their esophagus and may develop gastroesophageal reflux disorder.

Although people suffering from anorexia nervosa may have emaciated figures, it is more difficult to identify people who suffer from bulimia because, by definition, their weight is in the normal or overweight range. In fact, if a bingeing and purging individual weighs less then 85 percent of what is considered to be their minimally healthy weight, the appropriate diagnosis becomes anorexia nervosa. However, despite the absence of easily observable physical features, bulimics often show detectable signs of the disorder. Bulimics may eat large

amounts of food with no weight change, frequently take trips to the bathroom after meals, make kitchen visits at night, and rigidly adhere to exercise routines. Unlike anorectics who typically lack insight into their problems, bulimics are often distressed by their symptoms and ashamed of their behaviors. In addition, people suffering from bulimia are traditionally more prone to impulsive behavior, which can be manifested through abuse of drugs and alcohol or risk-taking behaviors. The comorbidity of bulimia with other psychiatric conditions is pronounced and includes anxiety disorders, major depression, dysthymia, substance use disorders, and personality disorders.

The age of onset for bulimia tends to correspond to late adolescence or early adulthood, slightly later in life than the onset of anorexia nervosa, which sometimes precedes the development of bulimia. In both clinical settings and general population studies, about 90 percent of identified bulimics are female. Among females in the general population, the prevalence of bulimia ranges from 1 percent to 3 percent, with even higher rates reported for college women. In westernized cultures, people of all backgrounds and ethnicities are affected by bulimia.

ONSET AND CAUSATION

The etiology of bulimia nervosa is multi-factorial, reflecting a combination of genetic, biological, and dispositional traits interacting with environmental risk factors to influence its development. Bulimia runs in families, and twin studies indicate a significant genetic contribution. Low self esteem, feelings of inadequacy, and a sense of lack of control over one's life may be contributing factors. Stressful life events, such as parental divorce and past sexual abuse, also confer increased risk for the development of bulimia. Cultural factors are also likely to be important, especially for women who embrace the images of ideal body types that are portrayed by modern media. These media messages glorify thinness and perpetuate narrow conceptions of beauty that include only women with certain body weights and shapes. The importance of such portrayals is borne out by studies that show that the prevalence of eating disorders is much higher in cultures in which the media play a large part in people's daily lives than in those cultures in which citizens are not exposed to many media forms. In addition, in less developed societies in which media influence has grown with modernization, the prevalence of eating disorders has increased.

TREATMENT

There are several different methods of treatment for bulimia nervosa, with preferred treatment involving a combination of therapies adjusted to meet the needs of the individual. Psychological treatment is likely to include cognitive behavioral therapy, with an additional emphasis placed on nutritional guidance and body image adjustment. Pharmacological treatment often involves antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs). In addition to being particularly helpful for bulimics with comorbid major depression or anxiety disorders, these medications also appear to reduce bingeing and purging, diminish the chances of relapse, and improve eating attitudes. The overlap of bulimia with substance abuse plus the compulsive nature of disordered eating has given rise to addiction models of eating disorders and twelve step treatment programs modeled after those developed for the treatment of substance dependence. However, these addiction models have proliferated in the absence of solid empirical support.

See also **Anorexia Nervosa; Overeating and Other Excessive Behaviors.**

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CAFFEINE. In the early twenty-first century, caffeine continues to be the most widely used psychoactive substance in the world. It can be found in a variety of dietary sources and medications, including coffee, tea, candy, soft drinks, and over-the-counter analgesics (pain medications) and cold remedies (Ogawa & Ueki, 2007). As a legal stimulant, caffeine is consumed daily by approximately 80 percent of the world's population, and it is available to both children and adults. Studies have shown caffeine consumption to be on the increase among children and adolescents in the United States. Average levels of daily caffeine consumption vary widely from country to country, with estimates for citizens of the United States and Canada averaging from 210 to 238 milligrams (mg)/person/day as compared to more than 400 mg/person/day for residents of Sweden and Finland. These daily dose levels are significantly higher than those shown to affect human behavior. For example, positive effects of caffeine on mood have been found at doses as low as 40 to 60 milligrams and positive effects on cognitive performance have been reported at a dose of 75 milligrams. Given that an 8 ounce serving of brewed coffee contains 135 milligrams of caffeine, an 8 ounce serving of green tea contains 30 milligrams of caffeine, a 1.5 ounce milk chocolate bar contains 10 milligrams of caffeine, and a 12-ounce cola drink contains 46 milligrams of caffeine, it is clear that people all over the world are consuming behaviorally active doses of caffeine on a daily basis.

CAFFEINE ABUSE/DEPENDENCE

The *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., *DSM-IV*) of the American Psychiatric Association does not list diagnoses of caffeine abuse or dependence, stating that insufficient clinical and research data were available in 1994 to support their inclusion among other substance use disorders. In the fifteen years since then, a number of reports were published demonstrating that a subset of the general adult population demonstrates clinical symptoms of caffeine abuse or dependence that are similar to those associated with other psychoactive substances such as alcohol and cocaine. For example, one survey-based study found that 44 percent of caffeine users endorsed at least three symptoms of caffeine dependence (Hughes et al., 1998).

A *DSM-IV* diagnosis of substance dependence requires that an individual meet at least three of the following seven criteria: (1) tolerance; (2) withdrawal; (3) intake of the substance in larger amounts or over a longer period of time than intended; (4) persistent desire or unsuccessful efforts to reduce intake or control use; (5) a great deal of time spent on the activities needed to obtain, use, or recover from the effects of the substance; (6) important social, occupational, or recreational activities are stopped or reduced because of substance use; and (7) continued use despite knowledge of a persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by the substance. The following sections consider these criteria in relation to caffeine.

Tolerance. In clinical studies of caffeine, one of the most frequently reported symptoms of dependence is tolerance. That is, regular caffeine users often report that the stimulant effects they initially experienced from a single cup of coffee now required consuming two or more cups of coffee to achieve the same effect. In addition to such anecdotal case reports, both human and non-human research studies have shown evidence of tolerance to the effects of caffeine. In animals, chronic caffeine administration has been shown to produce partial tolerance to various effects of caffeine and can produce complete tolerance to caffeine's stimulating effect on locomotor activity (involving movement from place to place) in rats. In humans, initial doses of 250 milligrams of caffeine can increase systolic and diastolic blood pressure. Tolerance to these effects develops quickly, however, often within four days. Less is known about tolerance to the central nervous system stimulant effects of caffeine. Indirectly, however, studies have shown that 300 milligrams of caffeine will often elicit self-reports of jitteriness in people who normally abstain from caffeine but will not elicit such statements from regular caffeine users.

Withdrawal. Another dependence criterion is the appearance of a withdrawal syndrome following abrupt termination of daily caffeine. Although there have been relatively few demonstrations of caffeine withdrawal in non-humans, abrupt termination of chronic daily caffeine has been shown clearly to decrease locomotor behavior in rats. Considerably more research on caffeine withdrawal has been done in humans. Anecdotal reports of caffeine withdrawal date back to the 1800s, with more systematic survey findings originating in the 1930s and continuing into the early twenty-first century. The cardinal symptom associated with caffeine withdrawal is a headache, which seems to develop gradually and can be throbbing and severe. Other caffeine withdrawal symptoms are fatigue (e.g., sleepiness, lethargy, drowsiness), depressed mood, and trouble concentrating. Some studies have also linked symptoms of anxiety to caffeine withdrawal.

Individual differences in the severity of caffeine withdrawal symptoms are considerable, ranging from mild to severe and such symptoms have been observed in persons consuming as little as 100 milligrams of caffeine per day. While withdrawal symptoms generally show a dose effect (e.g., more severe symptoms with higher levels of baseline use), variability is clearly present. In research with persons who were unaware they were experiencing caffeine withdrawal, some individuals experienced symptoms they reported as incapacitating (e.g., inability to go to work or care for children). In humans, caffeine withdrawal typically begins 12 to 24 hours after the last intake of caffeine, peaks at 20 to 48 hours, and can last from two to seven days. As with other drugs, caffeine suppresses caffeine withdrawal symptoms in a dose-dependent manner, so that the magnitude of suppression increases as the caffeine dose is increased.

The other dependence criteria often endorsed by regular caffeine users include a persistent desire or unsuccessful efforts to cut down or control use and continued use despite knowledge of a persistent or recurrent physical or psychological problem that is likely to be caused or exacerbated by continued use. In one study of caffeine use in pregnant women, more than half (57%) met *DSM-IV* criteria for dependence on caffeine (lifetime) and 45 percent reported a persistent desire or unsuccessful efforts to cut down or control use (Svikis et al., 1998). Another study with adolescents found that nearly one-fourth (21%) endorsed at least three of the seven *DSM-IV* criteria for dependence (Bernstein et al., 1998). Less frequently endorsed criteria for dependence on caffeine include considerable time spent on activities needed to obtain, use, or recover from its effects and giving up important social, occupational, or recreational activities to use caffeine. Clearly, these latter symptoms are more applicable to illicit drugs of abuse.

In one review of caffeine abuse and dependence, researchers indicated that despite its absence from *DSM-IV*, it is important for clinicians and practitioners to recognize that their patients may be dependent on caffeine and that some may experience distress as a function of being unable to control or stop their use. The authors advocate for practitioners to educate patients about possible sources of caffeine and how it may contribute to their medical or psychological problems. They also recommend that companies that sell or market products containing caffeine should indicate clearly the caffeine content of their products; warn about

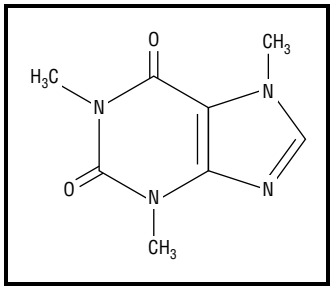


Figure 1. The caffeine molecule. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

limiting consumption by infants and children; and affirm that long-term consumption of large quantities of caffeine can lead to medical problems.

CLASS AND CHEMICAL STRUCTURE

Caffeine is an alkaloid that is often classified as a central nervous system stimulant. Caffeine is structurally related to xanthine, a purine molecule with two oxygen atoms (see Figure 1). Several important compounds, including caffeine, consist of the xanthine molecule with methyl groups attached. A methyl group consists of a carbon atom and three hydrogen atoms. These methylated xanthines, called methylxanthines, are differentiated by the number and location of methyl groups attached to the xanthine molecule. Caffeine is a 1, 3, 7-trimethylxanthine. The *tri* refers to the fact that caffeine has three methyl groups. The *1, 3, 7* refers to the position of the methyl groups on the purine molecule. Other important methylxanthines are theophylline, theobromine, and paraxanthine. All of these methylxanthines are metabolites of caffeine. In addition, theophylline and theobromine are ingested directly in some foods and medications.

Sources. Coffee and tea are the world's primary dietary sources of caffeine. In North America, approximately three-fourths of dietary caffeine comes from coffee. Elsewhere, tea is the most widely consumed beverage (after water), with black tea use more prevalent in Europe, North America, and North Africa, and green tea use more prevalent in Asia. Other sources of caffeine are cocoa products, cola beverages and so-called energy drinks. Caffeine is found in more than sixty species of plants. Coffee is derived from the beans (seeds) of several species of Coffea plants, and the leaves of Camellia sinensis plants are used in caffeine-containing teas. Chocolate comes from the seeds or beans of the caffeine-containing cocoa pods of Theobroma cacao trees. Table 1 shows the amounts of caffeine found in common dietary and medicinal sources. As shown in the table, the range of values for each shows how substantially caffeine content can vary depending on such factors as method of preparation or commercial brand.

Source	Standard value (in milligrams)	Minimum (in milligrams)	Maximum (in milligrams)
Coffee (6 oz/180 ml)			
ground roasted	102	77	186
instant	72	35	211
decaffeinated	4	2	10
Tea (6 oz/180 ml)			
leaf or bag	48	34	58
instant	36	29	37
Cola soft drink (12 oz/360 ml)	43	2	58
Energy drink (Jolt, 12 oz; Red Bull, 8.3 oz)	100	67	100
Chocolate milk (6 oz/180 ml)	4	2	5
Chocolate bar (1.45–1.75 oz/ 40–50 g)	7	5	31
Caffeine-containing over-the-counter medications			
analgesics and cold preparations	32	15	100
appetite suppressants and stimulants	100	50	350

Table 1. Caffeine content in common dietary and medicinal sources. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Effects on Mood and Performance. A substantive literature exists reporting the positive effects of caffeine at doses of 30 to 60 milligrams (see Smith 2005 for review). In particular, research has shown that caffeine use is correlated with improved performance on tasks that require sustained attention and effort. Although less robust, other studies have shown that low doses of caffeine (less than 200 mg) have a positive effect on speed of response and increase the person's positive sense of self-worth, with better concentration as well as higher levels of energy, self-confidence, alertness, and motivation. Interestingly, much of the research has focused on caffeine in coffee. Fewer studies have focused on caffeine in tea, although research as of 2008 has yielded generally similar findings. Higher doses of caffeine have been shown to improve or disrupt performance of complex tasks and increase physical endurance, work output, hand tremor, and reports of nervousness, jitteriness, restlessness, and anxiousness. Caffeine has also been associated with increased

production of cortisol and epinephrine, adrenal hormones that are secreted in response to stress. Consequently, it is suggested that caffeine intake may lead to exaggerated responses to the stressful events of normal daily life and, thus, contribute to an increased risk for cardiovascular disease.

DISCOVERY

Caffeine, derived from natural caffeine-containing plants, has been consumed for centuries by various cultures. Consumption of tea was first documented in China in 350 CE, although there is some evidence that the Chinese first consumed tea as early as the third century BCE. Coffee cultivation began around 600 CE, probably in what later became Ethiopia.

Caffeine was first chemically isolated from coffee beans in 1820 in Germany. By 1865, caffeine had been identified in tea, maté (a drink made from the leaves of a South American holly), and kola nuts (the chestnut-sized seed of an African tree).

THERAPEUTIC USES

Caffeine can be found in a variety of over-the-counter preparations marketed as analgesics, stimulants, cold remedies, decongestants, and menstrual-pain relievers. As an ingredient in analgesics, caffeine is used widely in the treatment of ordinary types of headaches, although evidence for caffeine's analgesic effects is limited. That is, caffeine may only diminish headaches caused by caffeine withdrawal. It should be noted, however, that caffeine has been combined with an ergot alkaloid in the treatment of migraines. In addition, there is some evidence to suggest that caffeine contributes to the constriction of cerebral blood vessels (Cornelis & El-Sohemy, 2007). Because of various effects of caffeine on the respiratory system, caffeine has historically also been used to treat asthma, chronic obstructive pulmonary disease, and neonatal apnea (transient cessation of breathing in newborns). Later, other agents such as theophylline were usually preferred for the treatment of asthma and chronic obstructive pulmonary disease.

ABUSE

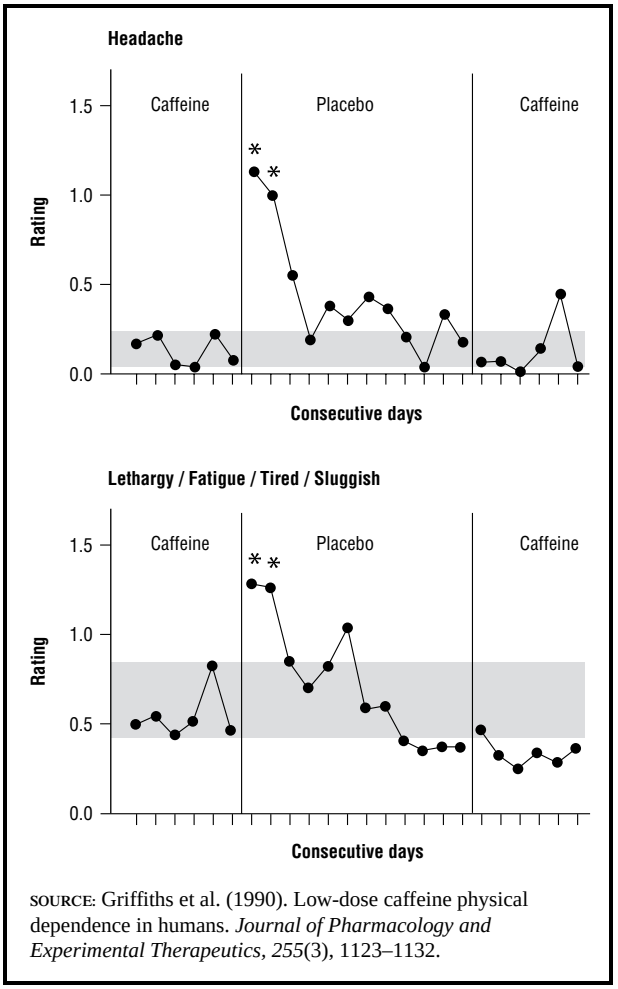
Strain and colleagues (1994) presented a number of case reports describing individuals who consume large amounts of caffeine—exceeding one gram per day (1,000 mg).While infrequent, such excessive intake, observed more frequently among psychiatric patients, drug and alcohol abusers, and anorectic patients, can produce a range of symptoms ranging from muscle twitching, anxiety, restlessness, nervousness, insomnia, rambling speech, tachycardia (rapid heartbeat), and cardiac arrhythmia (irregular heartbeat), as well as psychomotor agitation and sensory disturbances such as ringing in the ears and flashes of light. The disorder characterized by excessive caffeine intake has been referred to as *caffeinism*. There is some suggestion that excessive caffeine consumption can be linked to psychoses and anxiety disorders. Substantial amounts of caffeine are also used by a small percentage of competitive athletes, despite specific sanctions against such use.

ETIOLOGY

Twin study research has shown that caffeine use begins at an earlier age than nicotine, alcohol, or other substance use. It appears that at age nine, monozygotic (MZ; identical twin) and dizygotic (DZ; fraternal twin) correlations for caffeine use are quite similar, suggesting family environment contributes substantively to patterns of use. Starting at age ten, however, MZ and DZ correlations diverge and then from age 20 to age 35, MZ twin correlations (0.45) substantially exceed those of DZ twins (0.25). This pattern supports genetic factors influencing patterns of caffeine consumption, since MZ twins have 100 percent of their genes in common; whereas DZ twins have, on average, only 50 percent of their genes in common. Other studies have shown that genetic factors play a role in problematic caffeine use as well (e.g., heavy use, tolerance, and withdrawal). Further, as of 2008 emerging evidence suggests a common genetic link between caffeine dependence, substance use disorders, and psychiatric comorbidities (Kendler et al., 2008).

SELF-ADMINISTRATION STUDIES

Abused drugs are reliably self-administered under a range of environmental circumstances by humans and most are also self-administered by laboratory animals. Caffeine has been self-injected by laboratory non-human primates and self-administered orally and intravenously by rats, but there has been considerable variability across subjects and across studies (Griffiths & Woodson, 1988). Human self-administration of



SOURCE: Griffiths et al. (1990). Low-dose caffeine physical dependence in humans. *Journal of Pharmacology and Experimental Therapeutics, 255*(3), 1123–1132.

Figure 2. Caffeine withdrawal. The termination effects of daily caffeine consumption. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

caffeine has been variable, as well; however, it is clear that human subjects will self-administer caffeine, either in capsules or in coffee, and even when they are not informed that caffeine is the drug under study. For example, heavy coffee drinkers given repeated choices between capsules containing 100 milligrams of caffeine or placebo under double-blind conditions (in which neither the subject nor the experimenter knows which capsules contain the active drug) showed clear preference for the caffeine capsules and, on average, consumed between 500 and 1,300 milligrams of caffeine per day. Experimental studies with low-to-moderate caffeine consumers have found that between 30 and 60 percent of those subjects reliably choose caffeine over placebo in blind-choice tests (Griffiths Bigelow, & Liebson, 1989). Subjects tend to show less caffeine preference as the caffeine dose increases from 100 to 600 milligrams, and some subjects reliably avoid caffeine doses of 400 to 600 milligrams.

The nature of and time course of effects of terminating daily caffeine consumption are summarized in Figure 2 and summarize findings from seven adult subjects. All followed a caffeine-free diet throughout the study and received identically appearing capsules daily. Prior to the study, subjects had received 100 milligrams of caffeine daily for more than 100 days. Placebo capsules were substituted for caffeine without the subjects' knowledge, and subjects continued to receive placebo capsules for twelve days, after which caffeine administration was resumed. The top panel of the figure shows that substitution of placebo for caffeine produced statistically significant increases (asterisks) in the average ratings of headache during the first two days of placebo substitution. Headache ratings gradually decreased over the next twelve days and continued at low levels during the final caffeine condition. The bottom panel of the figure shows that the substitution of placebo for caffeine produced similar time-limited increases in subjects' ratings of lethargy/fatigue/tired/sluggish.

ORGAN SYSTEMS

Caffeine affects the cardiovascular, respiratory, gastrointestinal and central nervous systems. Most notably, caffeine stimulates cardiac muscles, relaxes smooth muscles, produces diuresis (urine production) by acting on the kidney, and stimulates the central nervous system. The potential of dietary doses of caffeine to stimulate the central nervous system is primarily inferred from caffeine's behavioral effects. Low-to-moderate caffeine doses can produce changes in mood (e.g., increased alertness) and performance (e.g., improvements in vigilance and reaction time), even in light, non-dependent caffeine users. Higher doses produce reports of nervousness and anxiousness, measurable disturbances in sleep, and increases in tremor. Very high doses can produce convulsions.

Consumption. Caffeine's cardiovascular effects are variable and depend on dose, route of administration, rate of administration, and history of caffeine consumption. Caffeine doses between 250

and 350 milligrams can produce small increases in blood pressure in caffeine-abstinent adults. Historically, it was thought that daily caffeine administration produced tolerance to these cardiovascular effects within several days, not affecting the blood pressure of regular caffeine users consuming comparable daily caffeine doses. However, later evidence suggests that blood pressure remains reactive to the pressor (blood pressure increasing) effects of caffeine in the diet and that caffeine use may substantially contribute to cardiovascular morbidity and mortality (Vlachopoulos et al., 2005). Chronic caffeine consumption has also been associated with increased aortic stiffness and wave reflections, which may further heighten the risk of cardiovascular disease. Additionally, a study involving a genetic marker of caffeine metabolism provided strong evidence that caffeine can contribute to the risk of coronary heart disease and myocardial infarction (Cornelis et al., 2006).

High caffeine doses can produce a rapid heartbeat (tachycardia) and in rare cases irregularities in heartbeat (cardiac arrhythmia). Caffeine's effects on peripheral blood flow and vascular resistance are variable. In contrast, caffeine appears to increase cerebrovascular resistance and decrease cerebral blood flow.

Moderate doses of caffeine can increase respiratory rate in caffeine-abstinent adults. Caffeine also relaxes the smooth muscles of the bronchi. Because of the effects of caffeine on respiration, it has been used to treat asthma, chronic obstructive pulmonary disease, and neonatal apnea (transient cessation of breathing in newborns).

Moderate doses of caffeine can act on the kidney to produce diuretic effects that diminish after chronic dosing. Caffeine has a variety of effects on the gastrointestinal system, particularly the stimulation of acid secretion. These effects can contribute to digestive upset and to ulcers of the gastrointestinal system. In addition, caffeine increases the concentration of free fatty acids in plasma and increases the basal metabolic rate.

TOXICITY

High doses of caffeine, typically doses above 300 milligrams, can produce restlessness, depression, anxiousness, nervousness, excitement, flushed face, diuresis, gastrointestinal problems, and headache. Psychiatric symptoms may also be exacerbated by caffeine use in individuals with schizophrenia. Doses above 1,000 milligrams can produce rambling speech, muscle twitching, irregular heartbeat, rapid heartbeat, sleeping difficulties, ringing in the ears, motor disturbances, anxiety, vomiting, and convulsions. Psychosis has also been noted in normal individuals who consume toxic doses of caffeine. Adverse effects of high doses of caffeine have been referred to as caffeine intoxication, a condition recognized by the American Psychiatric Association. Extremely high doses of caffeine—between 5,000 and 10,000 milligrams—can produce convulsions and death.

Extremely high doses of caffeine, well above dietary amounts, have been shown to produce teratogenic effects (birth defects) in mammals (Griffiths & Woodson, 1988). Although there is some evidence to the contrary, dietary doses of caffeine do not appear to affect the incidence of malformations or of low-birth-weight offspring. Although there has been some suggestion that caffeine consumption increases the incidence of benign fibrocystic disease of the breast and cancer of the pancreas, kidney, lower urinary tract, and breast, associations have not been clearly established between caffeine intake and any of these conditions.

Controversies continue over the medical risks of caffeine. Although research has not definitively resolved all the controversies, health-care professionals must make recommendations regarding safe and appropriate use of caffeine. In one survey of physician specialists, more than 65 percent recommended reductions in caffeine in patients with arrhythmias, palpitations, tachycardia, esophagitis/hiatal hernia, fibrocystic disease, or ulcers, as well as in patients who are pregnant (Hughes, Amori, & Hatsukami, 1988).

Prenatal Caffeine Use. Historically, caffeine use during pregnancy has been associated with a variety of adverse consequences, most notably miscarriage and low birth weight. The U.S. Food and Drug Administration recommended that "Women who are pregnant or planning to get pregnant should speak with their doctor about using caffeine." In general, the literature suggested that practitioners advocate that pregnant women limit their caffeine

use to less than 300 milligrams per day. One study with 1,063 women, however, yielded inconsistent findings, noting that as little as 200 milligrams per day was associated with increased risk of miscarriageng (Weng, Odouli, & Li, 2008). Compared to nonusers, women who consumed up to 200 milligrams of caffeine daily had an increased risk of miscarriage (15% vs. 12%), and the risk doubled for women consuming more than 200 milligrams daily (25%), even after controlling for potential confounders. Clearly, the safest advice a practitioner can give a pregnant woman is to abstain from caffeine use during pregnancy, particularly in the first trimester.

PHARMACOKINETICS

Absorption and Distribution. Caffeine can be effectively administered orally, rectally, intramuscularly, or intravenously; however, it is usually administered orally. Orally consumed caffeine is rapidly and completely absorbed into the bloodstream through the gastrointestinal tract, producing effects in as little as fifteen minutes and reaching peak plasma levels within an hour. Food reduces the rate of absorption. Caffeine readily moves through all cells and tissue, largely by simple diffusion, and thus is distributed to all body organs, quickly reaching equilibrium between blood and all tissues, including brain. Caffeine crosses the placenta, and it passes into breast milk. Many drugs interact with caffeine and since most individuals use multiple substances, this is important to recognize.

Metabolism and Excretion. The bloodstream delivers caffeine to the liver, where it is converted to a variety of metabolites. Most of an ingested dose of caffeine is converted to paraxanthine and then to several other metabolites. A smaller proportion of caffeine is converted to theophylline and theobromine; both of those compounds are also further metabolized. Some of these metabolites may contribute to caffeine's physiologic and behavioral effects.

The amount of time required for the body of an adult to remove half of an ingested dose of caffeine (i.e., the half-life) is three to seven hours. On average, about 95 percent of a dose of caffeine is excreted within 15 to 35 hours. Cigarette smoking produces a twofold increase in the rate at which caffeine is eliminated from the body. There is a twofold decrease in the caffeine elimination rate in women using oral contraceptive steroids and during the later stages of pregnancy. Newborn infants eliminate caffeine at markedly slower rates, requiring over 10 days to eliminate about 95 percent of a dose of caffeine. By one year of age, a child's caffeine elimination rates increase substantially, exceeding those of adults; school-aged children eliminated caffeine twice as fast as adults.

MECHANISMS OF ACTION

Three mechanisms by which caffeine might exert its behavioral and physiological effects have been proposed: (1) blockade of receptors for adenosine; (2) inhibition of the activity of phosphodiesterase (an enzyme) resulting in the accumulation of cyclic nucleotides; and (3) translocation of intracellular calcium (Griffiths & Woodson, 1988). Only one of these, however, the blockade of adenosine receptors, occurs at caffeine concentrations in plasma produced by dietary consumption of caffeine. Adenosine (an autacoid, or cell-activity modifier), found throughout the body, has a variety of effects that are often opposite to caffeine's effects. Because caffeine is structurally very similar to adenosine, it can bind to the receptor sites normally occupied by adenosine, thereby blocking adenosine binding and preventing adenosine's normal activity. Thus, caffeine's ability to stimulate the central nervous system and increase urine output and gastric secretions may be due to the blockade of adenosine's normal tendency to depress the central nervous system and decrease urine output and gastric secretions. The methylxanthine metabolites of caffeine (including paraxanthine, theophylline, and theobromine) are also structurally similar to adenosine and block adenosine binding.

See also **Addiction: Concepts and Definitions; Chocolate; Coffee; Tolerance and Physical Dependence.**

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CALCIUM CARBIMIDE. Citrated calcium carbimide is a mixture of two parts citric acid to one part calcium carbimide; it slows the metabolism of alcohol (ethanol) from acetaldehyde to acetate, so it is used in the treatment of alcoholism. It is also known as calcium cyanamide. As an antidipsotropic—an antialcohol or alcohol-sensitizing medication, it has been used for treatment in Canada, the United Kingdom, and Europe since its introduction for clinical use in 1956. Its only therapeutic use is for the treatment of alcoholism. In Canada it is sold under the brand name Temposil. As of 2000, however, calcium carbimide is still not approved for use in the United States.

PHARMACOLOGY

The pharmacokinetic data on the absorption metabolism and elimination of carbimide in humans are incomplete. Since nausea, headache, and vomiting occur because of the rapid absorption of carbimide, for treatment purposes it is formulated as a slow-release tablet. Peak plasma concentrations of carbimide following oral administration in experimental animals occur at 60 minutes; the drug is then metabolized at a relatively rapid rate so that half disappears about every 90 minutes (i.e., an apparent elimination half-life of 92.4 minutes). In humans, an alcohol challenge reaction will occur on an average of 12 to 24 hours after drinking.

Alcohol (ethanol) is normally metabolized first to acetaldehyde, which is then quickly metabolized further so that levels of acetaldehyde are ordinarily quite low in the body (acetaldehyde is toxic). Carbimide produces competitive inhibition of hepatic (liver) aldehyde-NAD oxidoreductase dehydrogenase (ALDH), the enzyme from the liver responsible for oxidation of acetaldehyde into acetate and water. Within two hours of taking carbimide by mouth, ALDH inhibition occurs. If alcohol is then ingested, blood acetaldehyde levels are increased; also mild facial flushing, rapid heartbeat, shortness of breath, and nausea occur with just one drink. As more is drunk, the severity of the reaction increases, with rising discomfort and apprehension. Severe reactions can pose a serious medical risk that requires immediate attention.

DOSAGE AND ADMINISTRATION

In Canada, Temposil is available as round, white 50-mg tablets engraved with the letters "LL" and "U13." The usual dosage is 50 or 100 mg every twelve hours. The drug should never be given to an intoxicated patient and preferably no sooner than 36 hours after the last drink.

Calcium carbimide should be used with caution in patients with asthma, coronary artery disease, or myocardial disease.

In the event of an overdose, the patient should be given pure (100%) oxygen by mask or antihistamines administered intravenously.

SIDE EFFECTS

Unlike disulfiram, carbimide does not have the potential side effect of liver damage. Carbimide, however, exerts antithyroid activity, which can be clinically significant in patients with preexisting hypothyroid disease. According to a 1999 Canadian monograph, other side effects of calcium carbimide include fatigue, skin rashes, ringing in the ears, mild depression, a need to urinate frequently, and impotence. The clinical significance of transient white blood cell increases remains unclear.

USE IN TREATMENT

The rationale for use of carbimide in alcoholism treatment is similar to that of disulfiram. The threat of an unpleasant reaction, which one may expect following drinking, is sufficient to deter drinking. For alcoholics in treatment who take a drink, the ensuing reaction is unpleasant enough to strengthen their overall conditioned aversion to alcohol. Their reduction of alcohol consumption during carbimide treatment is expected to result in general bodily improvement. A second approach involves the use of carbimide as part of a relapse-prevention treatment, whereby an individual might take it in anticipation of a high-risk situation. As of 2000, scientific evidence supporting the efficacy of carbimide in alcoholism treatment is inconclusive because of a lack of well-controlled clinical trials. No multicenter clinical trials have yet been performed.

See also **Risk Factors for Substance Use, Abuse, and Dependence: Learning; Treatment, Pharmacological Approaches to: Aversion Therapy; Treatment, Pharmacological Approaches to: Disulfiram.**

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CANADA. From the founding of the nation onward, alcohol and drugs have been vexing problems in Canada. Despite difficulties, important strides have been made in dealing with such problems. Persistent, sometimes brilliant, efforts at prevention, treatment, and legal controls have made all the difference. Fortunately, Canada has a long history of research on alcohol and drug abuse and methods for controlling it.

HISTORY OF USE

When explorers and settlers came to Canada in the 1600s, they found small, scattered populations of Indians and Inuit. These peoples had no indigenous psychoactive drugs, and they had not discovered alcohol. Some groups smoked various grasses, but they had little nicotine or other drugs. Many, but not all, native Canadians took easily to alcohol, and it quickly became a problem. Alcohol was often used as barter in the fur trade with native groups to get better prices. Many native groups had a tradition of "eat it all" feasts because food could not be preserved. For some this soon became "drink it all" feasts with drunkenness and wild behavior. Earlier settlers also drank heavily as many social events had free alcohol, and pubs were often the first buildings put up in new settlements.

Temperance movements held down alcohol consumption in the 1800s, especially for Methodist and Presbyterian settlers. Prohibition during the 1930s also controlled alcohol problems. Prohibition in Canada, however, was enacted at the provincial level, never by the federal government, and did not last very long in most places. Alcohol and tobacco consumption increased greatly in the years after World War II.

Drugs such as coca and opiates were available in many over-the-counter preparations in the early 1900s, but legislation soon did away with them. Heroin, other opiates, and cannabis were largely unknown in Canada before the 1960s, and cocaine became popular only in the 1980s.

PATTERNS AND TRENDS

In Canada alcohol, tobacco, cannabis, and cocaine are the most prevalently used and abused drugs. A 2004 national survey found that 79.3 percent of adults were drinkers, 7.2 percent were lifetime abstainers, and 13.5 percent were former drinkers. Since 1989 the proportion of drinkers has increased slightly (from 77.7 to 79.3%). About seven percent usually drank five or more drinks per occasion in 2004; 14.8 percent found that alcohol had adversely affected their health; 8.1 percent, their marriages or home life; and 6.9 percent, their finances. All these harmful results had increased between 1989 and 2004 for adults. However, students' alcohol use declined between 1999 and 2007, along with some alcohol problems.

About 20 percent of adults in Canada smoked cigarettes in 2004, but the rate declined slightly in the following few years. Among students, very large declines occurred between 1999 and 2007 in the numbers who smoked tobacco (28.4 to 11.99%).

In 2004 about 44.5 percent of adults reported some illicit drug use in their lifetime, but no trend data are available. In that 2004 survey, 14.1 percent reported using cannabis in the past year; 1.9 percent, cocaine or crack; and less than 1 percent, LSD, speed, or heroin. 1.19 percent had used Ecstasy (MDMA, or methylenedioxymethamphetamine). About 10.1 percent reported harm to their physical health from illicit drug use in the past year, and 5.1 percent reported harm to their home life. Among students aged 14 to 18, drug use declined between 1999 and 2007 for virtually all illicit drugs except cannabis. Cannabis use continued to

increase among students—about 26 percent used it at least once in 2008. Also, more students reported cannabis use and driving than reported drinking and driving. Use of solvents and binge drinking has shown no decline among students. Use of OxyContin is becoming a problem for some students; this drug is often found in parents' prescriptions, which students use illicitly.

Traditionally Canada was an importer of illicit drugs, but now it is also a producer. Many cannabis-growing operations were found from 2003 to 2008. In addition, numerous labs for making Ecstasy were closed by police. In 2006 some 5.2 million Canadian-made Ecstasy pills were seized. Canada now exports cannabis and ecstasy to the United States, Asia, and Europe, according to police reports.

CONSEQUENCES

Although some declines have been seen, serious physical and social consequences from drug and alcohol use remain a problem in Canada. These consequences include death, injuries, admissions to treatment, and impaired driving.

Statistics Canada estimates yearly deaths due to alcohol to be 6,507, with 1,146 due to motor vehicle accidents, 1,037 due to liver cirrhosis, and 9,555 due to suicide. In addition 82,100 admissions to hospitals occurred because of alcohol. There were 34,728 deaths attributed to tobacco, with 12,151 for lung cancer, 6,671 for chronic obstructive pulmonary disease, and the remainder for other diseases. There were 194,000 estimated admissions for tobacco-related cases. Finally, there were only 805 deaths due to illicit drugs, with 329 for suicide, 160 for poisonings, and 61 for AIDS. Only 6,940 admissions to hospitals were attributed to illicit drugs. Clearly smoking creates a far greater health burden for society than does alcohol or other drugs. It should be noted, too, that alcohol reduces some death rates from heart disease and hence creates some benefits that tobacco and illicit drugs lack.

Research has shown that in Ontario, the largest province, rates of both alcohol and drug problems declined in the period 1975 to 1990. For example, heavy alcohol consumption, liver cirrhosis, hospital admissions, and impaired driving all declined substantially, with liver cirrhosis rates declining by 32 percent and drinking and driving mortality by 57 percent. These reductions have been attributed to greatly increased prevention and treatment efforts. This includes a tripling of numbers of alcoholics treated, a doubling of the numbers in Alcoholics Anonymous, more alcohol education, and more health prevention programs for workers. However, in the early twenty-first century, alcohol consumption increased again, whereas impaired driving charges remained stable or increased somewhat. Canada experienced a long wave of heavy consumption after World War II, then a long wave of decreased consumption, followed by a shorter wave of stability in alcohol consumption. Whether the future portends another long wave of heavy consumption is unclear, but there are a few unsettling signs.

The trend in impaired driving in Canada has been going downward for many years. In 2008 there were about 30,000 convictions for impaired driving in Canada. The peak years for impaired driving were in the late 1970s; convictions have declined by more than 50 percent since that time. The decline was largely due to the passage of a law in Canada that made 0.08 the legal limit for blood alcohol concentration and mandated a variety of other prevention and legally based programs for impaired drivers. The 0.08 law was well-publicized, and for the first time police had a portable breath tester. Other measures include longer jail terms and larger fines for impaired drivers. Reductions in alcohol-related deaths and injuries on the road in Canada represent a real success for both public health and the law.

Similar successes have been found with tobacco smoking. During the 1950s about half of Canadian adults smoked cigarettes. However, the 2008 rate is around 20 percent, and most smokers smoke fewer cigarettes. Death rates from lung cancer have fallen dramatically since the 1980s and 1990s. Much of this decline is due to government health warnings about smoking, the restrictions on smoking in public places such as restaurants and theaters, and large tax increases on tobacco products. The cost of cigarettes has more than tripled since the late 1980s. There is, however, a large black market in cigarettes. Canadian tobacco companies a few years ago sold cigarettes at low prices through native reservations, but the government stopped

this. Some Indian reservations make "native" cigarettes and sell them at about half the price of regular cigarettes. They represent a significant problem in reducing levels of smoking in Canada.

An important consequence of alcohol and drug use is that people need treatment for their addictions. Good estimates of how many people were recently treated for addiction in Canada are difficult to obtain. The number of treatment agencies and clinics is large; there is no set definition of treatment, or of addiction. Actual counts were made for Ontario in 1992, when about 50,000 people were treated for alcohol problems. By 2007 that number had increased somewhat. About 5.2 percent of adults in Ontario met the criteria for alcohol addiction. Also, in the 2007 Ontario school survey, 19 percent of students met the criteria for hazardous drinking, and 15 percent had a drug problem. About 1.5 percent of students reported being treated for an alcohol or drug problem at some time during the past year.

Most Canadians can obtain treatment for alcohol and drug problems, except those in isolated small communities. The national health care system means most medical treatment is free. Also, many employee-based assistance programs provide access to care for addicted employees. Most addiction treatment in Canada is done on an outpatient basis (about 80%). Several Canadian studies have shown that outpatient and inpatient treatment achieve similar improvement rates. Inpatient treatment for addiction can be difficult to obtain except in large centers with specialized inpatient care.

ALCOHOL AND DRUG REGULATIONS

Canada has a complex federal system of government. There are 10 provinces, plus northern territories, and the federal government in Ottawa. The federal government is responsible for legislation on illicit drugs, most of the laws on impaired driving, and some of those on smoking. Provincial governments make all legislation on the sale and distribution of consumer products, such as alcohol and tobacco; hence, multiple regulations govern the sale of alcoholic beverages and nicotine in all forms. The federal government has overall control over the national health plan, which is universal and prepaid. However, health care is delivered by provincial health systems through hospitals, clinics, and private professionals. This system makes it difficult to create a national picture of what is happening in the area of addictions. For example, it is impossible to have a national view of how many alcoholics or drug addicts are in treatment or what treatment they are receiving.

Traditionally, regulation in the addictions area can be summarized as hard on drugs, but easy on alcohol and tobacco. Canada entered the drug wars of the 1970s and 1980s by arresting and criminalizing many drug users, but few importers and dealers. Access to alcohol was constantly made easier by lowering age limits, reducing prices, and many other aspects of alcohol control. However, in the 1990s to 2008, alcohol liberalization slowed, and controls on tobacco purchasing increased, along with prices for tobacco products. Also cannabis legislation was modified to reduce criminal penalties for possession and to allow discharges for convictions. Cannabis growing and importing, however, remain serious crimes. The use of cannabis for medical purposes is now allowed, albeit under strict regulation.

NATIONAL AND INTERNATIONAL PERSPECTIVES

Canada has often been at the forefront of efforts to prevent, control, and treat the consequences of drug and alcohol use. One of the first international drug treaties was organized by Bishop Brent, a Canadian clergyman. The Shanghai Opium Convention was the first to get international control over narcotics; Brent and others were the main organizers for this convention. Since that time Canada has supported and signed all major drug control treaties. Canadian policy makers and scientists have often participated in legal and health commissions and organizations concerned with alcohol and drug problems. The first head of the World Health Organization was a Canadian physician and Canadian experts have often been involved in WHO planning and its work at the international and country levels.

The future prospects for controlling alcohol and drug abuse nationally are difficult to discern at present. There are many hopeful portents; for example, there is a long-term decline in alcohol consumption and related problems. Smoking rates

are also down substantially. Drug use among youth is on a long-term downward trend. However, cannabis use has not declined among students, and cannabis and driving is now more common than drinking and driving. Also, use of OxyContin has increased as students take their parents' prescription drugs from the medicine chest. Continued vigilance and action will be needed to make sure that cannabis and OxyContin do not become larger problems.

See also **Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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CANCER, DRUGS, AND ALCOHOL.

DISEASE BURDEN ATTRIBUTABLE TO ALCOHOL

The World Health Organization's 2000 Comparative Risk Assessment Study (see Ezzati et al., 2004; Lopez et al., 2006; Rehm et al., 2004), found alcohol to be one of the most important risk factors for the global burden of disease, with alcohol ranking fifth, just behind tobacco (the alcohol-attributable burden was 4.0% of the global burden, compared to 4.1% for tobacco). Only underweight resulting from malnutrition and underfeeding, unsafe sex, and high blood pressure (which ranked first, second, and third, respectively) had more impact on the burden of disease than tobacco and alcohol (World Health Organization, 2002).

In 2002, 3.7 percent of all deaths worldwide were attributable to alcohol (6.1% for men; 1.1% for women). In addition, 4.4 percent of all disability-adjusted life years (7.1% for men; 1.4% for women) were attributable to alcohol (Rehm et al., 2006). (These percentages are net numbers that take into account the cardioprotective effect of alcohol.)

CARCINOGENESIS

In studies in which water containing ethanol is administered to laboratory animals, a dose-related increase has been noted in hepatocellular adenomas and carcinomas (U.S. National Toxicology Program, 2004); in head and neck carcinomas, fore-stomach carcinomas, testicular interstitial-cell adenomas, and osteosarcomas of the head and neck (Soffritti et al., 2002); and in mammary adenocarcinomas in female rats (Watabiki et al., 2000). The carcinogenic effect also increased when the ethanol was co-administered with known carcinogens.

The conversion of alcohol (ethanol) to acetaldehyde (the major metabolite of alcohol) in the liver requires the enzyme alcohol dehydrogenase, and acetaldehyde is transformed to acetic acid by the enzyme aldehyde dehydrogenase. Deficiencies in aldehyde dehydrogenase (which is most common among those of Asian descent) result in high levels of accumulated acetaldehyde in the body, which contribute to the development of malignant esophageal tumors (Baan et al., 2007; International Agency for Research on Cancer, 2007).

ALCOHOL AND CANCER

Comparative risk analyses and calculations on the alcohol-attributable burden of disease have revealed that cancer deaths worldwide are the third largest category of deaths caused by alcohol consumption (after unintentional injuries, at 25.9%, and cardiovascular disease, at 23.3%), accounting for 18.7 percent of alcohol-attributable deaths among men in 2002 (Rehm et al., 2006). Among women, the single largest category of alcohol-attributable deaths was cancer deaths, which accounted for 25.0 percent of deaths caused by alcohol consumption.

In February 2007, the Working Group of the International Agency for Research on Cancer (IARC), which comprises 26 scientists from 15 countries, confirmed that research evidence has shown that alcoholic beverages are carcinogenic to humans. Specifically, the group confirmed the causality between alcohol consumption and the occurrence of the following malignant neoplasms: oral cavity, pharynx, larynx, esophagus, liver, colorectum, and female breast cancer (Baan et al., 2007; International

Malignant neoplasms	ICD-10	Reference to meta-analyses and reviews	Effect	Causality
Lip & oropharyngeal cancer	C00-C14	English et al. (1995); Single et al. (1996, 1999); Sjögren et al. (2000); Gutjahr et al. (2001); Ridolfo & Stevenson (2001) *There are enough data to calculate relative risk for subcategories of disease, e.g. Bagnardi et al. (2001); Corrao et al. (2004)*	Detrimental	Confirmed
Esophageal cancer	C15	English et al. (1995); Single et al. (1996, 1999); Sjögren et al. (2000); Gutjahr et al. (2001); Ridolfo & Stevenson (2001); Rehm et al. (2004); Corrao et al. (2004)	Detrimental	Confirmed
Stomach cancer	C16	Bagnardi et al. (2001) *It was concluded that inconsistencies in research provide inadequate evidence that alcohol causes stomach cancer (English et al., 1995; Baan et al., 2007; IARC, 2007).*	Detrimental	Unclear (inconsistent results)
Cancer of small intestine	C17	Baganardi et al. (2001)	Detrimental	Not confirmed
Colon cancer	C18	Bagnardi et al. (2001); Corrao et al. (2004); Cho et al. (2004); Moskal et al. (2007); Bofetta & Hashiba (2006). *The IARC identified colorectal cancer as causally related to alcohol drinking in its meeting in February 2007 (Baan et al., 2007; IARC, 2007).*	Detrimental	Confirmed
Rectal cancer	C20	Bagnardi et al. (2001); Corrao et al. (2004); Cho et al. (2004); Moskal et al. (2007); Bofetta & Hashiba (2006). *The IARC identified colorectal cancer as causally related to alcohol drinking in its meeting in February 2007 (Baan et al., 2007; IARC, 2007).*	Detrimental	Confirmed
Liver cancer	C22	English et al. (1995); Single et al. (1996, 1999); Sjögren et al. (2000); Bagnardi et al. (2001); Gutjahr et al. (2001); Ridolfo & Stevenson (2001); Rehm et al. (2004); Corrao et al. (2004)	Detrimental	Confirmed
Gallbladder cancer	C23	Baganardi et al. (2001)	Detrimental	Not confirmed
Pancreatic cancer	C25	Baganardi et al. (2001)	Detrimental	Not confirmed
Laryngeal cancer	C32	English et al. (1995); Single et al. (1996, 1999); Sjögren et al. (2000); Gutjahr et al. (2001); Ridolfo & Stevenson (2001); Rehm et al. (2004); Bagnardi et al. (2001), Corrao et al. (2004), Altieri et al. (2005)	Detrimental	Confirmed
Lung cancer	C34	*This was excluded from the list of diseases causally related to alcohol. This decision has not been revised through any further meta-analysis. Meta-analyses on alcohol and lung cancer found only a borderline significant result (Bagnardi et al. 2001; Freudenheim et al., 2005) and the last substantive reviews found no sufficient support for a causal relationship (Bandera et al., 2001; Wakai et al., 2007).*	Detrimental	Unclear (inconsistent results)
Female breast cancer	C50	Single et al. (1996, 1999); Sjögren et al. (2000); Bagnardi et al. (2001); Gutjahr et al. (2001); Ridolfo & Stevenson (2001); Rehm et al. (2004); Singletary (2003); Hamajima et al. (2002); Corrao et al. (2004); Key et al. (2006); Singletary & Gapstur (2001); Ellison et al. (2001); Smith-Warner et al. (1998). *English et al. (1995) concluded that there was only limited evidence for causality; although they found a consistent relationship, subsequent studies using the same criteria have concluded that there is sufficient evidence of a relationship (Baan et al., 2007; IARC, 2007).*	Detrimental	Confirmed
Ovarian cancer	C56	Bagnardi et al. (2001) *English et al. (1995), consistent with IARC (1988), have concluded inadequate evidence that alcohol causes ovarian cancer*	Detrimental	Not confirmed
Prostate cancer	C61	Bagnardi et al. (2001)	Detrimental	Not confirmed
Kidney cancer	C64	Hu et al. (2003); Hsu et al. (2007)	Beneficial	Lack of carcinogenicity (Inverse trend)
Bladder cancer	C67	Bagnardi et al. (2001b)	Detrimental	Not confirmed
Non-Hodgkin's lymphoma	C82-C83	Morton et al. (2005); Besson et al. (2006)	Mainly beneficial or no effect	Lack of carcinogenicity (Inverse association or no association)

Table 1. Association between alcohol consumption and cancer as identified by various meta-analyses and reviews. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Agency for Research on Cancer, 2007). Furthermore, lack of carcinogenicity was confirmed for renal-cell cancer and non-Hodgkin's lymphoma. Evidence on causality between alcohol consumption and risks of other types of cancer was sparse or inconsistent. (These results are summarized in Table 1.) In addition, the working group concluded that there is "sufficient evidence" for the carcinogenicity of ethanol in animals, and it classified the ethanol in alcoholic beverages as carcinogenic to humans

Cancer of the Upper Digestive Tract (Oral Cavity, Pharynx, Larynx, and Esophagus). Causality for these cancers was confirmed during the first IARC Monographs meeting on the evaluation of carcinogenic risks of alcohol to humans (IARC, 1988). Studies showed that daily consumption of approximately 50 grams of ethanol increases the risk for these cancers two to three times, compared with the risk for abstainers. The effects of drinking and smoking were found to be multiplicative.

Liver Cancer. Causality for liver cancer was also confirmed during the first IARC Monographs meeting. The evidence suggests that the consumption of alcohol is an independent risk factor for primary liver cancer.

Breast Cancer in Women. Causality for breast cancer was also confirmed. Based on several epidemiological studies, each additional 10 grams (less than one standard drink) of alcohol per day is associated with an increase of 7.1 percent in the relative risk (RR) of breast cancer (Hamajima et al., 2002), though this risk is possibly higher (Key et al. estimated it at 10% in 2006). Even for regular consumption of about 18 grams of alcohol per day, the increase in RR is statistically significant. Hamajima et al. reported that about 4 percent of the female breast cancer cases in developed countries may be attributable to alcohol consumption. The mechanism of association between alcohol and breast cancer may involve increased levels of estrogen (Boffetta & Hashibe, 2006; Foster & Marriott, 2006) or increased levels of plasma insulin-like growth factor (IGF) produced by the liver due to moderate consumption of alcohol (Yu & Berkel, 1999).

Colorectal Cancer. A causal relation between alcohol and colorectal cancer has been established by the IARC (Baan et al., 2007). Research studies provide evidence for an increased relative risk of about 1.4 percent for colorectal cancer with regular consumption of about 50 grams of alcohol per day, compared with abstainers. This association is similar for both colon cancer and rectal cancer (Cho et al., 2004; Moskal et al., 2007).

Moskal and colleagues (2007) estimated a 15 percent increase in the risk of colon or rectal cancer for an increase of 100 grams (about 7 standard drinks) of alcohol per week. Low folate intake increases the risk of colorectal cancer, and alcohol could act through folate metabolism or synergistically with low folate intake to increase the risk, however the effects may be moderate (Boffetta & Hashibe, 2006). Moskal and associates also suggested a genotoxic effect of acetaldehyde, a metabolite of alcohol, and genetic polymorphism in subjects as factors for enhancing the risk of colorectal cancer.

Kidney Cancer. Evidence shows no increase in risk for renal-cell cancer with increasing alcohol consumption. Several studies have reported that increased alcohol consumption was associated with a significantly lower risk for renal-cell cancer for both men and women (Hu et al., 2003; Hsu et al., 2007).

Non-Hodgkin's Lymphoma. Several studies have demonstrated an inverse association or no association between alcohol consumption and non-Hodgkin's lymphoma. The majority of the studies show a lower risk in drinkers than in abstainers (Morton et al., 2005; Besson et al., 2006).

Lung Cancer. As evidence for a possible biological mechanism was not conclusive, and residual confounding from smoking could not be excluded, it was decided to exclude lung cancer from the list of diseases influenced by alcohol.

Stomach Cancer. The association of stomach cancer with the consumption of alcoholic beverages is not confirmed. Epidemiological studies show inconsistent results and the interpretation of the findings is not clear.

TOBACCO AND CANCER

The role of tobacco as a carcinogen is well established and described elsewhere.

Malignant neoplasms	ICD-10	Reference to meta-analyses and reviews	Effect	Causality
Oropharyngeal cancer	C00-C14, D00.0	English et al. (1995)	Detrimental	Confirmed
Esophageal cancer	C15, D00.1	English et al. (1995)	Detrimental	Confirmed
Stomach cancer	C16, D00.2	Tredaniel et al. (1997)	Detrimental	Confirmed
Pancreas cancer	C25, D01.9	English et al. (1995)	Detrimental	Confirmed
Laryngeal cancer	C32, D02.0	English et al. (1995)	Detrimental	Confirmed
Trachea, bronchus and lung cancers	C33-C34	Simonato et al. (2001)	Detrimental	Confirmed
Cervical cancer	C53, D06	Plummer et al. (2003)	Detrimental	Confirmed
Urinary tract cancer	C64-C68	Zeegers et al. (2000)	Detrimental	Confirmed
Renal cell carcinoma	C64	Hunt (2005)	Detrimental	Confirmed
Bladder cancer	C67, D09.0	Brennan et al. (2000; 2001)	Detrimental	Confirmed
Acute myeloid leukemia	C92.0	Brownson et al. (1993)	Detrimental	Confirmed

Table 2. Association between tobacco and cancer as identified by various meta-analyses and reviews. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

In 2004, the U.S. Surgeon General added the following diseases to the list of those for which evidence is sufficient to conclude a causal relationship between smoking and disease: stomach cancer, renal cell carcinoma, uterine cervical cancer, and pancreatic cancer. (For the full list of the malignant neoplasms casually associated with tobacco, see Table 2.)

ILLEGAL DRUGS (MARIJUANA) AND CANCER

In many countries, marijuana is the second most commonly smoked substance (after tobacco), and it is considered to be the least risky among the various illegal drugs. However, there is a concern that smoking marijuana may be a risk factor for tobacco-related cancers, because the smoke of marijuana, like that of tobacco, contains a number of the same carcinogens. However, smoking marijuana may actually be more harmful than smoking tobacco, since more tar is inhaled and retained when smoking marijuana.

Several studies support the biological plausibility of an association of marijuana smoking with lung cancer on the basis of molecular, cellular, and histopathologic findings. However, the role of marijuana as a risk factor for lung cancer is difficult to assess because most marijuana smokers are also tobacco smokers. The epidemiologic evidence that marijuana smoking may lead to lung cancer is limited and inconsistent (Mehra et al., 2006; Hashibe et al., 2005, 2006).

An IARC study reviewed several epidemiological studies that assessed the association of marijuana use and cancer risk including lung, head and neck, colorectal, non-Hodgkin's lymphoma, prostate, cervical cancers, and glioma (Hashibe et al., 2005). Due to methodological limitations in the existing studies—including selection bias, possible underreporting where marijuana use is illegal, small sample sizes, limited generalizability, and too few heavy marijuana users in the study samples—the authors concluded that the reviewed studies are not adequate to evaluate the impact of marijuana use on cancer risk. In view of the growing interest in medicinal marijuana, further epidemiologic studies are needed to clarify the true risks of regular marijuana smoking on cancer and other health conditions.

See also **Alcohol: Chemistry and Pharmacology; Cannabis Sativa; Complications: Immunologic; Complications: Liver (Clinical); Epidemiology of Alcohol Use Disorders; Epidemiology of Drug Abuse; Tobacco: Medical Complications.**

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SVETLANA POPOVA
JÜRGEN REHM

CANNABINOIDS. Cannabis or marijuana has been used for thousands of years for medicinal, religious, and recreational purposes (Mechoulam et al., 1991). Extracts of this plant material were first introduced to Western Europe from India for medicinal purposes in the middle of the nineteenth century by William O'Shaughnessy, a British physician.

Marijuana is the most widely used illegal drug in the United States (Johnston et al., 2007) and many individuals believe that it should be legalized for medicinal purposes. Its primary psychoactive constituent, δ^9-tetrahydrocannabinol (δ^9-THC), has already been approved by the U.S. Food and Drug Administration as a synthetic oral formulation (called dronabinol) to treat nausea and vomiting related to the chemotherapy administered to cancer patients and as an appetite stimulant for AIDS patients.

δ^9-THC belongs to a class of drugs called cannabinoids, which despite great structural diversity (Figure 1), produce pharmacological effects similar to those of marijuana. In addition to the 60 to 70 cannabinoids that have been identified in marijuana, chemists have synthesized hundreds of cannabinoid analogs that vary greatly in their pharmacological potency including the highly potent compounds WIN55,212-2 and CP-55,940. Another major cannabinoid present in marijuana, cannabidiol (CBD), is structurally similar to δ^9-THC, though it lacks psychoactivity (Figure 1). An oromucosal (mouth) spray containing equal parts of δ^9-THC and CBD, known as Sativex, has been approved in Canada to treat pain and spasticity in multiple sclerosis patients.

In humans, cannabinoids produce a constellation of pharmacological and psychological effects including increased heart rate, reddened conjunctivae (the clear membranes covering the white part of the eye), impaired short-term memory, increased appetite, mild euphoria, perceptual alterations, time distortion, and intensified sensory experiences. Similarly, in laboratory animals, cannabinoids reliably produce a variety of effects including hypomotility (decreased activity of the gut), catalepsy (muscular rigidity), decreased pain sensitivity, hypothermia (decreased body temperature), memory impairment, and increased heart rate.

ENDOGENOUS CANNABINOID SYSTEM

Beginning in the early 1990s a series of discoveries revealed the existence of a naturally occurring cannabinoid system in humans and animals known as the endogenous cannabinoid (endocannabinoid) system. This system is comprised of two different receptors that have been identified and cloned, endogenous ligands (chemicals that bind to the receptors and activate them) and enzymes regulating the biosynthesis and degradation of these ligands (Ahn et al., 2008). CB_1 cannabinoid receptors are expressed throughout the central nervous system in brain regions regulating learning and memory, feeding, pleasure, emotionality, pain, and motor behavior, as well as in the periphery (Herkenham et al., 1991). These receptors are predominantly located presynaptically where their stimulation generally inhibits the release of neurotransmitters including GABA, glutamate, and acetylcholine throughout the central nervous system. In contrast, CB_2 cannabinoid receptors are primarily located in peripheral tissues, though these receptors are also present on microglial cells in the brain and are also expressed at low levels in brainstem neurons. While CB_1 cannabinoid receptors are responsible for the central nervous system (CNS) effects of cannabinoids, CB_2 cannabinoid receptors are associated with immune responses and their stimulation generally elicits anti-inflammatory effects. The availability of CB_1 (e.g., rimonabant) and CB_2 (e.g., SR144528) receptor antagonists has been useful in determining the receptor mechanism of action of different cannabinoids (Figure 1). Of note, rimonabant (Acomplia) has been medically approved in Europe and Mexico as a weight-loss drug for obese patients.

The two best characterized endocannabinoids that bind to and activate both cannabinoid receptors are n-arachidonoyl ethanolamine (anandamide), which is translated from the word "eternal bliss" in Sanskrit, and 2-arachidonoyl glycerol (2-AG), both of which vary greatly in structure from other cannabinoids (Figure 1). In contrast to classical neurotransmitters, which are stored in synaptic vesicles and released from the presynaptic neuron following an action potential, these lipid signaling molecules are enzymatically produced in the postsynaptic neuron upon demand through a calcium-dependent process and travel retrogradely (in a reverse direction) to the presynaptic neuron where they inhibit neurotransmitter release (Ahn et al., 2008). Following their

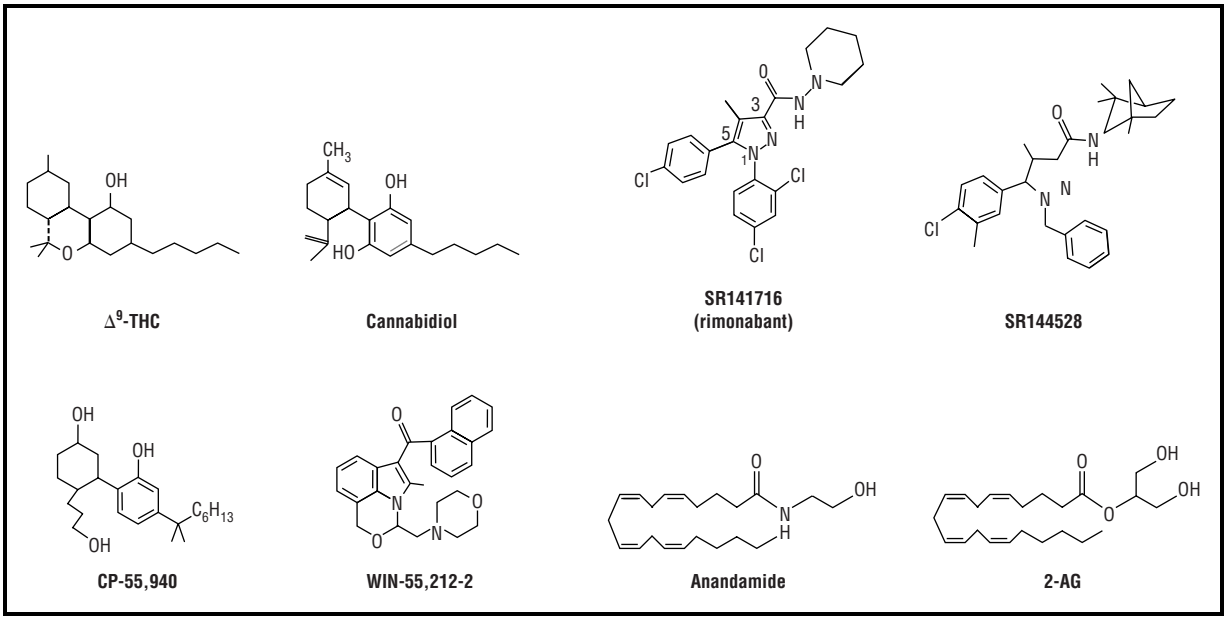

Figure 1. Structures of naturally occurring cannabinoids (Δ^9-THC and cannabindiol), synthetic cannabinoid analogs (CP-55,940 and WIN-55,212-2), the selective CB_1 antagonist rimonabant, the selective CB_2 receptor antagonist SR144528, and endogenous cannabinoids (anandamide and 2-AG). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

release, both anandamide and 2-AG are rapidly broken down. Anandamide degradation is regulated primarily by fatty acid amide hydrolase (FAAH), while monoacylglycerol lipase (MGL) and, to a lesser extent, α/β-hydrolase 6 and α/β-hydrolase 12, are responsible for 2-AG catabolism. Two *sn*-1-specific diacylglycerol lipases ($DAGL_\alpha$ and $DAGL_\beta$) have been identified that can produce 2-AG. Initially the sequential actions of an *N*-acyl phosphatidyl ethanolamine-producing transacylase and a phospholipase D were hypothesized to regulate anandamide biosynthesis. However, genetically modified mice lacking this enzyme displayed normal endocannabinoid levels thus ruling out a direct role of these enzymes in anandamide biosynthesis. Alternative enzymatic pathways for anandamide biosynthesis are currently under investigation.

PHYSIOLOGICAL FUNCTION

Through the use of genetically altered mice and specific drugs that either disrupt or augment endocannabinoid signaling, accumulating evidence indicates that the endogenous cannabinoid system modulates a wide range of physiological processes (Pacher et al., 2006) including feeding, regulation of body weight, learning and memory, neuroprotective mechanisms from excitotoxic insults and traumatic brain injury, pain and inflammation, and substance abuse. CB_1 knockout mice as well as wild type mice that are treated with CB_1 receptor antagonists display decreases in food intake and lipogenesis (the synthesis of fatty acids) through distinct central and peripheral mechanisms. Drugs blocking CB_1 receptors also reduce behavioral effects of a variety of drugs including opioids (e.g., morphine), nicotine, and alcohol in laboratory animals. Additionally, endogenous cannabinoids are produced and released on demand to dampen the damage caused by brain injury or seizures in animal models. Drugs preventing the breakdown of the endocannabinoids reduce pain and inflammation as well as elicit antidepressant-like and anti-anxiety-like effects in laboratory animals. Finally, the endogenous cannabinoid system appears to modulate a specific type of learning called extinction in which learned behavior is suppressed when reinforcement is withheld (Lutz, 2007). Specifically, disruption of CB_1 receptor signaling disrupts the ability of mice to extinguish behaviors that are associated with aversive, but not positive, memories.

POTENTIAL

Cannabinoids are a diverse class of drugs that produce effects similar to those produced by marijuana.

The endogenous cannabinoid system modulates a wide variety of behaviors and physiological processes. A great deal of research is focused on elucidating the function of the endogenous cannabinoid system, and exploring its potential as a target for new pharmacotherapies.

See also **Cannabis; Cannabis Sativa; Marijuana (Cannabis).**

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ARON H. LICHTMAN

CANNABIS, INTERNATIONAL OVERVIEW.

The marijuana plant Cannabis sativa contains a bewildering array of organic chemicals, with representatives of almost all chemical classes present, including mono- and sesquiterpenes, carbohydrates, aromatics, and a variety of nitrogenous compounds. Interest in the study of this plant has largely focused on the resinous matter, as it is this material that is invested with the pharmacological activity peculiar to the plant. This resin is secreted by the female plant as a protective agent during seed ripening, although it can be found as a microscopic exudate through the aerial portions of plants of either sex. The pure resin, hashish or charas, is the most potent part of the plant and has served as the source material for most chemical studies. The family of chemicals isolated from this source has been referred to as the cannabinoid group.

The production of cannabinoids and their associated terpenes in cannabis is subject to environmental factors as well as hereditary determinants. Their biosynthesis occurs in specialized glands populating the surface of all aerial structures of the plant. These compounds apparently serve as defensive agents in a variety of antidessication, antimicrobial, antifeedant, and UV-B pigmentation roles. In addition, the more intense ambient UV-B of the tropics, in combination with the UV-B lability of cannabidiol, may have influenced the evolution of an alternative biogenetic route from cannabigerol to tetrahydrocannabinol in some varieties. Delta-9-tetrahydrocannabinol (THC) is the cannabinoid responsible for the main psychoactive effects of most cannabis drug preparations. THC is thought to be produced by the plant from cannabidiol (CBD) that, in turn, is derived from cannabigerol (CBG) generated from noncannabinoid precursors. It was isolated in 1964 by Raphael Mechoulam, Yechiel Gaoni, and Habib Edery of the Weizmann Institute in Rehovot, Israel. The pharmacological actions of THC result from its binding to the cannabinoid receptor CB1 located in the brain. These specialized receptors in the brain are for endogenous cannabinoids manufactured by the body such as anandamide, 2-arachidonyl glyceride (2-AG), and other related compounds. These cannabinoids have a natural role in pain modulation, control of movement, and memory. The natural role of cannabinoids in immune systems remains unclear. The brain develops tolerance to cannabinoids and animal research demonstrates the potential for dependence, but this potential is observed under a narrower range of conditions than exist for benzodiazepines, opiates, cocaine, or nicotine.

MEDICAL USE AND SIDE EFFECTS

As bewildering as the array of organic chemicals is the variety of claims made for cannabis and cannabinoids. THC may be an effective anticancer treatment, with studies from 1975 and 2007

showing tumor reduction in mice. A two-year study in which rats and mice were force-fed tetrahydrocannabinol dissolved in corn oil showed reduced body mass, enhanced survival rates, and decreased tumor incidences in several sites, mainly organs under hormonal control. It also caused testicular atrophy and uterine and ovarian hypoplasia, as well as hyperactivity and convulsions immediately after administration. In mice, low doses of THC reduce the progression of atherosclerosis. A U.K.-based company, GW Pharmaceuticals, has developed Sativex, a cannabinoid pharmaceutical product, that is administered as an oral spray to be absorbed by the patient's mouth. In April 2005 the company received regulatory approval for the sale of this product in Canada for the symptomatic relief of neuropathic pain in multiple sclerosis and as an adjunctive analgesic treatment in patients with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain.

On the other end of the spectrum, in 2007 *The Lancet* published a study indicating that cannabis users have, on average, a 41 percent greater risk of developing psychosis than nonusers. The risk was most pronounced in cases with an existing risk of psychotic disorder and was said to increase to 200 percent for the most frequent users. Some early-twenty-first-century research has also shown a correlation between cannabis use and increased cognitive function in schizophrenic patients.

EARLIER USE AND EFFORTS TO CONTROL

Although considerable debate surrounds the medical benefits and health risks of using cannabis products, there is no doubting their potential as a recreational drug. Details of cannabis' use in premodern Asian, African, and Arabic societies are difficult to rely on for various reasons, including, for example, the confusion between the terms *hashish* (cannabis), *afyūn* (opium), and *banj* (drugs) in medieval Islamic law. However, by the time Europeans began to observe consumption in these regions in the nineteenth century, it was clear that cannabis substances were varied and enjoyed multiple roles as medicines, tonics, and intoxicants. Local attitudes toward cannabis preparations were similarly varied, so that on the one hand they were embraced in marriage rituals and religious festivals, and on the other they were featured in cautionary rhymes, such as the following from Sind, a poet from an historic area now within the borders of Pakistan:

> It is not charas but a curse.
> It burns the chest and heart to its worse.
> It brings on dimness of the eyes.
> To phlegm and cough it must give rise.
> To blind the eyes it never fails.
> Or cripple limbs that once were hale.
> In what but death, ends its sad tale?

Premodern governments adopted a variety of positions toward cannabis-consuming societies. Mughal administrators in eighteenth-century India sought to raise revenue by taxing trade in its preparations, while at one point in Egypt a prohibition was enforced whereby users of cannabis faced having their teeth pulled out as punishment for indulgence in the drug. Western governments first confronted the task of governing cannabis-consuming societies in the eighteenth century as parts of Asia and Africa became incorporated within European empires. Yet little consistency emerged as imperial administrators tended to adopt and adapt policies put in place by their predecessors. This led to a contradiction within the British Empire, for example, where officials in India remained content to allow locals to consume cannabis after paying a duty on it, while their counterparts in Egypt insisted on a complete ban. At one point, smugglers bought cannabis from the British in Bombay only to smuggle it into Egypt past the British officers of the Coastguard Camel Corps.

The international drug regulatory system that binds together all members of the United Nations (UN) within a common legal framework on intoxicating substances, including cannabis, had its origins in the politics of empire. Cannabis was first included in these regulations as a result of the 1925 meeting of the League of Nations in Geneva to discuss new opium controls. The substance had been scarcely featured in discussions about drugs before World War I in Shanghai or the Hague, and had been rarely mentioned in debates under the auspices of the League of Nations before 1925. However, at the 1925 meeting, the Egyptian delegate, Mohamed El Guindy, described cannabis as a "scourge which reduces man to the level of the brute and deprives him of health and reason, self-control and honour." Cannabis was not on the agenda for the League's second opium convention

but a number of countries rallied to the Egyptian cause, particularly the United States. That country's delegation had little interest in the subject of cannabis, which was not viewed as a problem at home in the 1920s, but instead sought allies for its controversial proposals on opium. The United States may also have been attracted to the Egyptian agenda: to embarrass the capitulary powers, the European states that exercised colonial control over Egypt. Despite the opposition of the United Kingdom and the British administration in India, which derived a sizable revenue from taxing cannabis consumption there, the International Opium Convention (the 1925 Geneva Convention) included the first international controls on cannabis thanks to Egypt's intervention.

These events in 1925 created the international control regime for cannabis under particularly curious circumstances. A body controlled largely by Western government officials decided to impose controls on substances mainly consumed by Asians, Africans, and some South Americans, most of whom were not consulted about this major policy move, and despite the fact that there was little evidence presented or informed discussion. Indeed, the decisions of 1925 also meant that Western governments found themselves formulating laws and designing control mechanisms for cannabis before a domestic market even existed for it. One can thus argue that control options were therefore severely limited when consumers did eventually materialize in the West.

The growth in Western markets for cannabis products began in the 1930s in the United States. There in the Southern states, Mexican migrant workers brought their cannabis-using habits with them, and they soon spread across the nation via out-of-work Americans traveling the country in search of employment during the Great Depression. Cannabis was cheap and readily available; it easily grew in the warm environment of the South and proved an attractive option to the poor who could not afford alcohol as a recreational drug. In the United Kingdom in the 1950s, migrant workers from the country's Asian and African colonies brought their cannabis use with them as they arrived to meet the demand for labor in the postwar economy. Again, the poorer members of the indigenous community took to the migrant's intoxicant during a period of domestic austerity.

MODERN USE AND EFFORTS TO CONTROL

The picture changed in the 1960s when cannabis was adopted as an emblem of the counterculture in Western countries. As the drug was an intoxicant most associated with Asians, Africans, and South Americans, it served as a ready symbol of the rejection of the orthodoxies of Western society by middle-class white youth. In the decades since, domestic markets for cannabis have increased in Western societies, although this has less to do with its place in the short-lived counterculture movements of the 1960s and more to do with the nature of the hybridized youth cultures that have developed in urban centers and attached meanings to customs perceived to be "black" or "African" in origin. One recent study indicated that in the United Kingdom about 20 percent of 16- to 24-year-olds had used cannabis in the last year, compared with approximately 9 percent of the general population. In the United States, almost 7 percent of the 12 to 17 age group had used cannabis in the last month, and across the population 6 percent indulged during that same timeframe, representing about 14.8 million people.

Regulatory responses to these consumers have been framed within an international drug control system that became more restricted after World War II. The 1950s were a decade in which the reputation of cannabis sank to a new low, with the World Health Organization stating in 1954 that "there is no justification for the medical use of cannabis preparations" (WHO, 1954, p. 10). The 1961 UN Single Convention on Narcotic Drugs had as its basic principle the notion that nonmedical consumption of drugs should be prohibited, and it aimed to control cannabis more tightly by closer definition of the various preparations of the drug.

The UN has continued to take a hard line on cannabis since then; it has sought to maintain a consensus on the drug when faced with independent actions by individual states. For example, in 2003 the United Kingdom decided to reclassify cannabis and Philip Emafo, then the head of the International Narcotics Control Board, responded by arguing that "no government should take unilateral measures without considering the impact of its actions and ultimately the consequences for an entire system that took governments almost a century to establish" (BBC News, 2003). However, it

is clear that most governments have moved away from severe sentences for possession of the smallest amounts of cannabis, which marked the 1960s.

Broadly speaking, the pattern in most Western countries is to limit the punishment for possession of small amounts of the drug that are most likely for personal consumption to warnings or small fines. More severe penalties are aimed at suppliers and traffickers of the drug. Possession usually remains an offense in these circumstances and, in effect, cannabis policy moves within the orbit of the police and the judiciary rather than politicians and legislators, as it is the discretion of the former that decides how cannabis users are treated. Since the 1960s a range of groups have emerged to represent all shades of cannabis consumers, from those who seek more ready access to the drug for medical reasons to those who seek to repeal all laws related to cannabis. As most Western governments have moved to a legal system where personal use rarely carries severe sentences, and as ongoing research into cannabis continues to reveal that its use may involve hazards as well as benefits, it is unlikely that groups campaigning for legalization will enjoy success in the near future.

See also **Cannabinoids; Cannabis Sativa; Epidemics of Drug Abuse in the United States; Hashish; International Drug Supply Systems; Marijuana (Cannabis); Tetrahydrocannabinol (THC).**

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JAMES MILLS

CANNABIS SATIVA. This is the botanical name for the hemp plant that originated in Asia. It is the basis of the hemp industry as well as the source of the widely used intoxicant tetrahydrocannabinol (THC), the active agent in marijuana, hashish, ganja, and bhang.

HISTORY

The use of *Cannabis sativa* has been recorded for thousands of years, beginning in Asia. It was known to the ancient Greeks and later to the Arabs, who, during their spread of Islam from the seventh to the fifteenth centuries, also spread its use across the Levant and North Africa. Some 200–300 million people are estimated to use cannabis in some form worldwide. Thus, it is not only one of the oldest known but also one of the most widely used mind-altering drugs.

Since the 1960s, the rise in its use in the United States has been enormous and associated with the youth movement and countercultural revolution. Although the drug was in use before that time, it was popular only in some ethnic and specialized groups (e.g., jazz musicians). By the 1990s, some 30–40 million Americans are estimated to have used it and a substantial number use it regularly—although since 1979 the number of youngsters initiated into its use has been declining after a steep rise with an increasingly lower age of first use.

BOTANY

Cannabis sativa grows in the tropical, subtropical, and temperate regions. It is generally considered a single species of the mulberry family (Moraceae) with multiple morphological variants (e.g., *Cannabis indica* or *Cannabis americana*). It is an herb of varying size; some are quite bushy and attain a height of 10 to 15 feet (3 to 4.6 m). Due to genetic differences, some plants produce strong fibers (but little THC) and others produce a substantial quantity of THC but weak fibers. The fiber-producer is grown commercially for cloth, rope, roofing materials, and floor coverings; this was cultivated as a cash crop in colonial America for such purposes (Hart, 1980). During World War II, when it appeared that the United States might be cut off from Southeast Asian hemp, necessary to

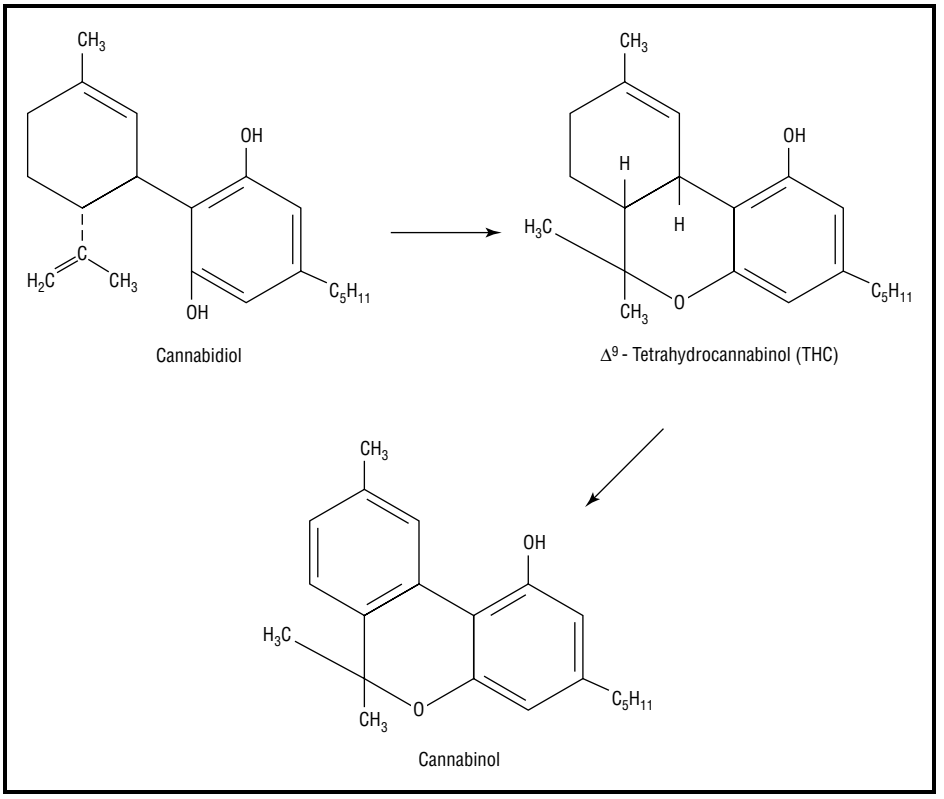

Figure 1. Biosynthetic pathway of cannabinoids. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

the war effort, the plants were cultivated in the mid-western states. Some of them continue to grow wild today, but since they are of the fiber-producing variety, they contain little drug content.

The drug-producing variety is widely cultivated in societies where its use is condoned. Illegal crops are also planted, some in the United States. The choice parts are the fresh top leaves and flowers of the female plant. The leaves have a characteristic configuration of five deeply cut serrated lobes. When they are harvested, they often resemble lawn cuttings—which accounts for the slang term "grass."

CHEMISTRY

The collective name given to the terpenes found in cannabis is *cannabinoids*. Most of the naturally occurring cannabinoids have now been identified, and three are the most abundant—cannabidiol (CBD), tetrahydrocannabinol (THC), and cannabinol (CBN). The steps from CBD to THC to CBN represent the biosynthetic pathway in the plant. THC is an optically active resinous material that is very lipid-soluble but water-insoluble; these physical properties make pharmacological investigations difficult, since various nonpolar solvents must be used. Although many other materials have been found in this plant, the cannabinoids are unique to it and THC is the only one with appreciable mental affects. THC is believed to be largely, if not solely, responsible for the effects desired by those who use cannabis socially. Virtually all the effects produced by smoking or eating some of the whole plant can be attained by using THC alone.

USE AS A SOCIAL DRUG

Cannabis grows so easily that it is called a weed. In the United States, where it remains illegal, it is possible for those who wish to use it as a social drug to grow their own supply. The ease of cultivation keeps the price of imported illicit marijuana down, which helps account for some of its widespread use. Such cultivation is, however, as illegal as possession of the drug obtained from illicit "street" sources.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Marijuana (Cannabis); Monitoring the Future; Tetrahydrocannabinol (THC).**

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CARIBBEAN, ILLICIT DRUGS IN.

Although the purview of this encyclopedia is all drugs, including alcohol and tobacco, the focus here is on marijuana, cocaine, and heroin, which are illegal substances that present a wide variety of societal and national security dangers for Caribbean countries. The dangers posed by these illicit substances threaten the stability and sovereignty of many of the nations in the region.

DIMENSIONS OF THE PROBLEM

Of the three substances mentioned above—marijuana, cocaine, and heroin—marijuana is the only substance produced in the Caribbean. The cultivation of marijuana varies among the region's countries. Belize, Guyana, Jamaica, St. Vincent and the Grenadines, and Trinidad and Tobago are among the countries with the highest levels of production. For decades, Jamaica had one of the highest levels of production and export, with the product being the nation's largest cash crop at times. *Ganja*, as marijuana is popularly called there and elsewhere in the Caribbean, is traditionally harvested after two main annual seasons of five- to six-month cycles. However, the *indica* variety matures in three or four months, making four harvests possible per year.

Economic conditions, the profitability of the drug market, geography, and the balloon effect of countermeasures in Belize, Jamaica, and Latin America (in which successful eradication efforts in one area only lead to increased production in another area, just as squeezing a balloon causes it to expand elsewhere) are among reasons that other Caribbean countries have taken to significant marijuana production and export, mainly to the United States. In the case of Guyana, for example, two principal features are conducive to myriad clandestine activities: physical geography and population density (with four people per square kilometer, Guyana has one of the lowest population densities in the world). It is therefore surprising that major marijuana cultivation did not begin there before the late 1980s.

Most of the marijuana cultivation in Trinidad and Tobago is done in the forested northern and central ranges and along the coast. As in Guyana and elsewhere, joint police-army operations, with notable support from the United States, are at the center of eradication and confiscation countermeasures. Elsewhere in the region, marijuana is cultivated in significant amounts in the Dominican Republic, French Guiana, Puerto Rico, St. Kitts-Nevis, and Suriname. As one might expect, there is variation in the size of plots cultivated—in some places production is primarily for domestic use, but in many areas the product is also grown for export.

The problem of narcotics consumption and abuse in the Caribbean involves mainly marijuana and cocaine, with heroin also being problematic in some places. Drug consumption and abuse in the region are not limited to any single social class or economic or ethnic group, although the consumption of certain drugs is higher in certain groups. Marijuana, for example, is predominantly the working-class drug of choice. Crack cocaine is widespread among the lower and middle classes because it has the attributes of being "hard" and a "status" drug, while also being inexpensive. Heroin, on the other hand, is a rich man's drug. Apart from the cost factor, the impact of heroin abuse in the region has been mitigated by a fear of using needles.

Like production, drug use differs from place to place. The greatest concern is in Jamaica, the Bahamas, the Dominican Republic, Guyana, Trinidad

and Tobago, and in parts of the eastern Caribbean. While marijuana is abused in many places, it has a long history of accepted socioreligious use dating back to the introduction of indentured workers from India following the abolition of slavery. Indeed, the word *ganja* is a Hindi word. Marijuana's socioreligious use patterns have changed over the years. This use is now associated primarily with the Rastafarians, Afrocentric social-religious sects that identify with the late Ethiopian emperor Haile Selassie (1892–1975). Hence, socioreligious usage is found in places with significant numbers of Rastafarians, including Jamaica, the eastern Caribbean, Guyana, and Trinidad and Tobago.

Cocaine abuse in the Caribbean is a result of the spillover from the illicit cocaine trade. Crack cocaine is readily available in many places, particularly in the principal transit states: the Bahamas, Jamaica, Belize, the Dominican Republic, Guyana, Puerto Rico, and Trinidad and Tobago. Needless to say, cocaine addiction can lead to singularly devastating acts, as in the 1994 case in Guyana in which a 30-year-old deranged crack addict murdered six people, including his own mother, in a machete attack in a village along the Atlantic Coast.

Apart from trading their own ganja in the United States, Canada, and Europe, some Caribbean countries are important transshipment centers for South American cocaine, heroin, and ganja bound for Europe and North America. For more than two decades, the Bahamas, Belize, and Jamaica dominated this business, but in the first decade of the twenty-first century the Dominican Republic, Guyana, Haiti, Trinidad and Tobago, and eastern Caribbean countries have featured more prominently, as the 2008 edition of the U.S. State Department's *International Narcotics Control Strategy Report* shows. For instance, the geography of the Bahamian archipelago makes it an excellent candidate for drug transshipment, given its 700 islands and strategic location in the airline flight path between Colombia and southern Florida.

The geography and topography of Belize also make that country ideal for drug smuggling. There are large jungle areas, sparse settlements, and about 140 isolated airstrips that facilitate stops on flights from South America to North America. Moreover, there is virtually no radar coverage beyond the 30-mile radius of the international airport at Belize City. There has been an increasing use of maritime routes in and out of Belize, however. Crack has also been featured more prominently in the country's trade. Several features of the Dominican Republic make that country a prime trafficking candidate as well, including proximity to Colombia, the Bahamas, Puerto Rico, and the southern United States; a long, often desolate, 193-mile-long border with Haiti; a coastline of nearly 1,000 miles; and poorly equipped police and military authorities. As for Jamaica, it has long been important to the drug trade, given its long coastline; proximity to the United States; its many ports, harbors, and beaches; and its closeness to the Yucatan and Windward passages. Trafficking takes place by both air and sea in Jamaica.

DRUGS AND SECURITY

Thus, what generally is called "the drug problem" in the Caribbean is really a multidimensional phenomenon with considerable societal and national security implications. However, the phenomenon does not present a security challenge merely because of its production, trafficking, and other dimensions. It does so essentially because of the following reasons: (1) these aspects of the drug trade have multiple consequences and implications, such as marked increases in crime, systemic and institutionalized corruption, and arms trafficking, among other factors; (2) drug operations and their consequences have increased in scope and gravity since the 1980s; (3) drug smuggling has a dramatic impact on agents and agencies of national security and good governance, in military, political, and economic ways; and (4) the sovereignty of many countries is subject to infringement, by both state and non-state actors, because of drugs.

In the 1980s, most Caribbean leaders found it impolitic to accept that their countries faced a drug threat. Over the years, however, the scope and severity of the threat increased and became patently obvious to observers within and outside of the region. Leaders could, therefore, no longer deny it. In June 2000, at a multinational high-level meeting on criminal justice in Trinidad and Tobago, that country's attorney general made the following declaration on behalf of the Caribbean:

> There is a direct nexus between illegal drugs and crimes of violence, sex crimes, domestic violence, maltreatment of children by parents and other evils. . . . Our citizens suffer from drug addiction, drug-related violence, and drug-related corruption of law enforcement and public officials. The drug lords have become a law unto themselves. . . . Aside from the very visible decimation of our societies caused by drug addiction and drug-related violence, there is another insidious evil: money laundering. . . . It changes democratic institutions, erodes the rule of law, and destroys civic order with impunity.

This statement by Attorney General Ramesh Lawrence Maharaj remains accurate and points clearly to the nexus between drugs and crime.

There is a local-global nexus in the region's drug-related crime, reflected in the fact that the crime is not all ad hoc, local crime; rather, some of it is transnational and organized, extending to North America, Europe, and elsewhere. Violent crime dramatizes the quotidian experiences of individual and corporate citizens in the Caribbean, reaching almost pandemic proportions in parts of the region. Indeed, a 2007 report by United Nations Office on Drugs and Crime (UNODC) and the World Bank indicated that murder rates in the Caribbean—at 30 per 100,000 population annually—were higher than in any other region of the world and had risen in recent years for many Caribbean countries. That study offers evidence of the wide-ranging economic, social, and other negative impact crime is having on the societies and nations in the region. In fact, as reported in an article titled "Crime Hurting Jamaica Tourism," in addressing the 47th Annual General Meeting of the Jamaica Hotel and Tourist Association in June 2008, Jamaica's Tourism Minister Edmund Bartlett averred dramatically, "Crime, in my mind, is the single most debilitating factor, the one area that is worrying to me beyond anything else, and I must tell you that the fuel crisis is not as worrying to me as crime. The turmoil in the aviation industry is not as worrying to me as crime."

Several aspects of drug-related crime are noteworthy. First, murder, fraud, theft, and assault are precisely the crimes likely to be associated with drugs. The experiences of the Bahamas, the U.S. Virgin Islands, Haiti, Guyana, Jamaica, Puerto Rico, Haiti, the Dominican Republic, and Trinidad and Tobago offer evidence of this. Clearly, then, drugs and crime are among the clear and present dangers facing the region. This was highlighted at the highest levels of the Caribbean Community (CARICOM) in April 2008, when the CARICOM leaders convened for a special security summit in Trinidad. Drug-related crime is even more important because it affects tourism, a national economic enterprise. Caribbean observers have known for some time what the *New York Times* declared in April 1994: Drug-related crime has transformed the "paradise" character of the U.S. Virgin Islands and other Caribbean vacation spots, driving fear into locals and tourists alike and depressing tourism (Rohter, 1994).

MULTIPLE RESPONSES

A range of measures are being adopted by states in the Caribbean to fight this problem. These measures are multidimensional, multilevel (national, regional, and international), and multi-actor. They need to be multidimensional because drug operations and their impact occur on many different dimensions. They need to be multilevel because drug operations and many of the problems they precipitate are both national and transnational. Moreover, they have to be multi-actor for the above reason and because Caribbean governments lack the necessary financial and other resources to meet the threats and challenges facing their nations. Hence, antidrug efforts require the involvement not only of governments but also of corporate bodies, nongovernmental organization (NGOs), and regional and international agencies such as the Regional Security System (RSS), the Organization of American States (OAS), the Inter-American Drug Abuse Control Commission (CICAD), and the U.N. Office on Drugs and Crime (UNODC).

The kind and impact of efforts introduced and maintained depend on three main factors: perceptions of the nature and scope of the predicament, national capacity, and foreign support. National efforts are wide-ranging in scope, if not sufficiently substantive in character. They include law enforcement, education, interdiction, demand reduction, rehabilitation, crop substitution, improved port management, better regulation of financial services, and legislation. Circumstances are such that measures cannot be undertaken only sequentially, however. Education, rehabilitation, interdiction, and the

other measures have to be applied at the same time. Indeed, in many places a misperception of the situation led to a failure to adopt simultaneous measures, which contributed to a worsening of the problem.

Foreign support is vital. Such assistance is not only bilateral, but multilateral as well, coming from the Europe Union, the OAS, and the UNODC, among other places. Most Caribbean countries have national drug councils that are supposed to set policy. They usually are composed of officials from various government agencies as well as NGOs and the private sector. The National Council on Drug Abuse (NCDA) of Jamaica, Programa para la prevención del uso indebido de drogas (PROPUID) of the Dominican Republic, the National Council for Drug Abuse Prevention (NaCoDAP) of the Netherlands Antilles, and the National Drug Council (NDC) of the Bahamas are a few examples of these bodies. Understandably, structures and operational efficiency vary from country to country.

In conclusion, it must be noted that all the Caribbean countries have joined the relevant international regimes, including the 1961 United Nations Single Convention on Narcotic Drugs; the 1971 Convention on Psychotropic Substances; and the 1988 Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances. Indeed, the Bahamas has the distinction of being the first country to ratify the 1988 convention, which it did on January 30, 1989. This convention includes provisions on drug trafficking, money laundering, organized crime, and arms trafficking, and it requires states to strengthen laws concerning financial reporting, extradition, asset forfeiture, and other subjects. It also urges adherents to improve cooperation in intelligence, interdiction, eradication, and other areas.

In terms of bilateral agreements, most Caribbean states have Mutual Legal Assistance Treaties (MLATs) with the United States. MLATs provide for training, joint interdiction, asset sharing, extradition, intelligence sharing, and material and technical support. Some countries, such as the Bahamas and Jamaica, have long had several complementary agreements with the United States. Bilateral treaties also exist with countries other than the United States. For instance, Belize has agreements with Mexico for intelligence sharing between the two, and for Mexican assistance with demand reduction and rehabilitation. Bilateral agreements also exist between Suriname and Colombia, Suriname and Guyana, Cuba and Guyana, Venezuela and Guyana, Jamaica and Mexico, Suriname and the Netherlands Antilles, Trinidad and Tobago and Venezuela, Cuba and Panama, and other sets of countries.

See also **Cocaine; Colombia; Drug Interdiction; Foreign Policy and Drugs, United States; Heroin; International Control Policies; International Drug Supply Systems; Marijuana (Cannabis); Mexico; U.S. Government: Agencies in Drug Law Enforcement and Supply Control.**

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IVELAW LLOYD GRIFFITH

CATECHOLAMINES. The catecholamines are a series of structurally similar amines (e.g., dopamine, epinephrine, norepinephrine that function as hormones, as neurotransmitters, or both. Catecholamines are produced by the enzymatic conversion of tyrosine, sharing the chemical root of 3, 4-dihydroxyphenylethanolamine. The three major catecholamines (mentioned above) derive from sequential enzymatic reactions—tyrosine is converted to dihydroxyphenylacetic acid (dopa); dopa, which is not an end product but a common intermediate (and the medication of choice for Parkinson's disease), is converted to dopamine; dopamine is converted to noradrenaline (also called norepinephrine); and noradrenaline is converted to adrenaline (also called epinephrine). These substances are the neurotransmitters for the sympathetic neurons (nerve cells) of the autonomic nervous system, as well as for three separate broad sets of brain neuropathways.

See also **Dopamine; Neurotransmitters; Norepinephrine.**

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FLOYD BLOOM

CAUSES OF SUBSTANCE ABUSE. *See* **Risk Factors for Substance Use, Abuse, and Dependence.**

CHEMISTRY AND PHARMACOLOGY OF ALCOHOL. *See* **Alcohol: Chemistry and Pharmacology.**

CHILD ABUSE AND DRUGS. To provide perspective on the issues discussed in this entry, a description of the extent of child abuse and neglect and drug abuse follows. Some of the ways in which child abuse and drugs may be related are then discussed. For example, exposure to alcohol and other drugs (AOD) may have an impact on the child pre- or postnatally. Parental substance abuse may affect parenting and increase the risk of child abuse. Having a history of child abuse may increase a person's risk of having a substance-abuse problem. And children of substance-abusing parents may engage in some form of abuse or neglect of their own offspring.

Child-abusing parents and substance-abusing parents share certain risk factors, such as poor parenting skills, family disorganization, involvement in criminal activity, and a disproportionately high incidence of mental and physical illnesses. Thus, children growing up in such households may be at risk of adverse developmental, social, behavioral, and health consequences. However, not all children exposed will manifest negative consequences. Some of these children will manage to cope effectively with such adversities and others will be helped by positive interventions.

EXTENT OF CHILD ABUSE AND NEGLECT

In 2006, according to information collected as part of the National Child Abuse and Neglect Data System overseen by the U.S. Department of Health and Human Services, state and local child protective service agencies investigated 3,573,000 million referrals for children reported to be abused or neglected. Of these, about 905,000 were determined to be victims of abuse or neglect, representing 1,210 per 100,000 children in the United States. Three-quarters of these children had no history of prior victimization. Approximately 64 percent of the children experienced neglect, 16 percent were victims of physical abuse, 9 percent were victims of sexual abuse, and 7 percent were victims of emotional or psychological maltreatment. During 2006 an estimated 1,530 children from 0 to 17 years old died as a result of abuse or neglect at a rate of 2.04 children per 100,000 in the national population.

These statistics represent only the reported cases. Research suggests that the number of victims of child abuse and neglect in the United States is much higher, with estimates varying depending on definitions of maltreatment and the age of the groups surveyed. In one national population-based survey of children's self-reports and caregiver reports, Finkelhor, Ormrod, Turner, and Hamby (2005) estimated that a total of 14 percent of children in the United States had experienced some form of child maltreatment; 75 percent were victims of emotional abuse, 48 percent physical abuse, 22 percent neglect, and 8 percent sexual abuse.

EXTENT OF DRUG ABUSE

According to the Substance Abuse and Mental Health Services Administration (SAMHSA, 2004), an estimated 21.6 million (9.1%) of people in the United States were considered to have a substance use disorder (SUD) in 2003. Of these, approximately 15 million had alcohol dependence, 4 million had drug dependence, and about 3 million had both alcohol and drug dependence disorders. Using data from the National Household Survey on Drug Abuse, SAMHSA (2003) estimated that 6 million children (9%) lived with at least one parent who abused or was dependent on alcohol or an illicit drug during the past year. Findings from the National Longitudinal Alcohol Epidemiologic Survey indicated that approximately 15 percent of children were living in households with one or more adults who currently abused or were dependent on alcohol, and 43 percent of children lived with one or more adults who had abused or been dependent on alcohol at some time in their lives (Grant, 2000). Based on this data, Grant estimated that approximately one-fourth of children are exposed to alcohol abuse or dependence in their families. In 2002 and 2003, 4.3 percent of pregnant women reported the use of illicit drugs during the past month and 4.1 percent reported binge alcohol use (SAMHSA, 2005). In one study of 36 hospitals, mainly in urban areas, Freier, Griffith, and Chasnoff (1991) reported prenatal exposure to illegal drugs in approximately 11 percent of all births each year. In sum, a substantial number of children are being exposed to substances and parental substance-abuse problems one way or another in the United States.

IMPACT OF DRUG EXPOSURE ON CHILDREN

A number of states legally define in utero exposure to alcohol and other drugs as child abuse. All 50 states require mandated reporting of suspected child abuse. Although the states differ in terms of who is identified as a mandatory reporter, in most states medical or social services personnel are mandated to report such cases to protective services workers (Liss, 1994). Because of concerns about the consequences of being reported, these mandatory reporting laws can result in the avoidance of prenatal care by substance-abusing pregnant women. For this reason, social services employees may hesitate to notify authorities. In addition, the notification of authorities may appear to be racially biased and discriminatory if more poor women of color are referred. Although researchers continue to debate the value of mandatory reporting laws (Margolin et al., 2005), the effectiveness of these laws is not known.

Alcohol may have teratogenic effects (resulting in abnormalities in the fetus) leading to fetal alcohol syndrome (FAS), alcohol-related neurodevelopmental disorder (ARND), or alcohol-related birth defects (ARBD). The effects of other drugs have also been studied, such as cocaine, methamphetamine, marijuana, opiates, and phencyclidine (PCP). Although some children who have been exposed to these drugs or alcohol may manifest immediate problems, including drug withdrawal and developmental delays, with good postnatal environments many of them can overcome their exposure in utero if systemic damage is not severe. The major effects of most drugs at birth are preterm deliveries of low-birth-weight infants, indicative of growth retardation that may affect both mental and physical development.

The quality of an infant's postnatal environment as actively constructed by the mother or caregiver appears to be the most significant factor in determining the impact of drugs on the drug-exposed or non-drug-exposed infant. Studies find that children born to drug-abusing mothers can look normal or be resilient to their in utero (prenatal) exposure to drugs if they are provided with a nurturing environment that includes responsiveness to their needs, stimulation, and early childhood education.

Few longitudinal studies have tracked the impact of drug exposure on children. The longest follow-up study is of prenatal opiate-exposed children evaluated

at 10 years of age. Moreover, it is very difficult to separate the impact of a poor postnatal environment from prenatal drug exposure (unless the children are adopted). The few longitudinal studies conducted of prenatal drug-exposed infants have determined that almost no long-term developmental problems are directly related to their drug exposure. A few cross-sectional studies of children of drug abusers have found clinically significant negative impacts on their emotional, academic, and behavioral status. These studies suggest that the greater the degree of maternal drug abuse, the greater the negative impact on the child's mental and behavioral status as measured by standardized clinical measures. One study, conducted by Adger (2000), found that children of alcoholics (COAs) are between four and nine times as likely to develop an alcohol use disorder as other children. These children are also at risk for other mental health problems, including internalizing problems such as depression and anxiety, as well as externalizing disorders such as attention deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder (Clark et al., 1997). Children of illicit drug abusers are more likely than other children to demonstrate immature, impulsive, or irresponsible behavior, and to have lower IQ scores and poorer school attendance. All these characteristics have been found to increase the risk of substance abuse.

Living with a parent who is actively abusing alcohol or other drugs causes stress for all family members, including very young children. Substance-abusing parents are often unable to be consistently available, either because of their own use or their concerns about their partner's use (Zucker, Ellis, Bingham, et al., 1996). The shame and stigma associated with substance-abuse problems makes their identification difficult, and often requires skillful screening, interviewing, and assessment of direct and indirect indicators.

Children can also be hurt by ingesting or inhaling alcohol and other drugs. Four major ways exist for children to become intoxicated: passive inhalation, accidental self-ingestion, being given drugs by a minor, and deliberate poisoning by an adult. In addition, infants can ingest alcohol, nicotine, and other drugs through breast milk. Passive inhalation of crack (freebase cocaine), PCP, marijuana, or hashish has negative effects.

The increase in methamphetamine abuse during the last decade, particularly among women of childbearing age, has led to reports of children being physically and emotionally neglected and exposed to serious environmental hazards, such as dirty needles and toxic materials. Children living with parents who manufacture synthetic designer drugs in their homes, such as methamphetamine, are exposed to hazardous toxic chemicals. Some substance-abusing parents allow their children to drink alcohol or use the drugs they find lying around the house. Some parents deliberately give their children alcohol or other drugs (i.e., tincture of opium) to reduce their crying, sedate them, or induce intoxication to amuse the parents. Any relatively healthy child with unexplained neurological symptoms, seizures, or death may have been exposed to drugs.

SUBSTANCE ABUSE AND RISK OF CHILD ABUSE

Child welfare authorities consider parental substance abuse to be a major risk factor for child abuse. An estimated 40 to 80 percent of the 3 million children who come to the attention of the child welfare system live in families with AOD problems (Young, Gardner, & Dennis, 1998). In addition, a 1997 Child Welfare League of America (CWLA) study of state child welfare agencies estimated that 67 percent of parents in the child welfare system required substance-abuse treatment services.

Under the influence of alcohol and other drugs, adults are less inhibited and have reduced judgment and emotional control. Uppers (stimulants such as cocaine, methamphetamine, PCP, and amphetamines) can cause anxiety, irritability, paranoia, and aggressiveness. Downers (depressants such as alcohol, opiates, sedatives, and barbiturates) have also been related to depression, irritability, and loss of control while disciplining children. It has been suggested that organic brain damage, hypoglycemia, and sleep disturbances caused by alcohol exacerbates child abuse by alcoholics. Substance-abusing parents are often irritable and angry because of neurochemical imbalances caused by persistent drug abuse.

Children of substance abusers are frequently more difficult to parent because of the increased prevalence of attention deficit disorder (ADD), hyperactivity, conduct disorders, and learning disorders. Some so-called difficult temperament characteristics

are caused by in utero exposure to drugs, some by genetic inheritance, and others by lack of nurturing and inconsistent parenting. However, these characteristics in children may place them at risk for being abused.

Psychosocial risk factors for child abuse include the following:

- *Poverty and Stress.* Many children of drug-abusing parents or caretakers are raised in poverty. Money that would normally be available for food, clothing, transportation, medical and dental care, and to provide social and educational opportunities for the children is often diverted to purchases of alcohol and drugs. Crack-addicted parents sometimes use food stamps and welfare checks to purchase crack. Lack of money to handle daily crises elevates the usual level of life stressors and increases parental anger and irritability. Unemployment, which frequently results in low self-esteem, can lead to increased child abuse.
- *Poor Parenting Skills.* Drug-abusing parents or caretakers have been found to have less adequate parenting skills, spend less time with their children, have unrealistic developmental expectations that can lead to excessive punishment, and lax or inconsistent discipline. Verbal abuse in the form of threatening, chastising, belittling, and criticizing are common.
- *Family Violence and Conflict.* High levels of family conflict found in drug-abusing families can lead to family violence, and drug abusers often belong to subcultures where violence is commonplace. The absence of empathy and support among family members in the home environment increases the risk of child abuse and family violence.
- *Mental Disorders.* Approximately 90 percent of drug abusers have other mental disorders, such as depression, bipolar-affective disorder, narcissism, antisocial personality, organic brain disease, and psychosis. Mental disorders of this nature can have a severe impact on a person's ability to parent and may lead to child abuse. Depression, bipolar disorder, and psychosis can cause parents to become angry, irrational, and abusive, whereas parents with personality disorders may be impulsive.
- *Physical Illness and Handicaps.* Physical illness and physical handicaps can reduce the patience parents need to handle the stress inherent in dealing with children. Physical illness is more common in substance-abusing families because of their lifestyle and lack of preventive health care. Intravenous drug abusers and their children have higher rates of common infections, as well as increased exposure to diseases transmitted through the blood (HIV/AIDS and hepatitis), sexually transmitted diseases (syphilis, gonorrhea, and herpes), and tuberculosis.
- *Criminal Involvement.* Drug-abusing parents are at high risk for criminal involvement by nature of their use alone or by the need to obtain considerable sums of money to support their habit. Prostitution, theft, and drug dealing are reported in about half of all drug-abusing parents. Arrest and incarceration may increase the stress on the family and can reduce inhibitions against sexual abuse upon reunification of the family.

Alcohol and drug use and abuse have also been directly implicated as risk factors for becoming abusive or neglectful. For example, some studies have reported a relationship between parental alcohol abuse and parental perpetration of physical child abuse (Chaffin, Kelleher, & Hollenberg, 1996; Kelleher, Chaffin, Hollenberg, et al., 1994; Kotch, Browne, Dufort, et al., 1999). Others have not found such an association, or the associations that were found were limited to certain subgroups of alcohol-using parents (Miller, Maguin, & Downs, 1997). In one 18-year longitudinal study of a New Zealand birth cohort, Woodward and Fergusson (2002) found that young people reared by mothers with a history of alcohol or drug problems and depression tended to report higher levels of their mother's use of physical punishment and child maltreatment during childhood (birth to age 16).

High rates of physical abuse have been reported in alcoholic and opiate-addicted families. In one study, conducted by Miller and co-workers (1997), mothers with histories of alcohol problems were more likely to report using harsh punishment on their children compared to women without such histories. Studies have also reported that parental drinking or

a family history of alcoholism was a risk factor for childhood sexual abuse. Miller and her colleagues also speculated that parental alcohol abuse may increase a child's vulnerability to sexual abuse by interfering with the parents' ability to provide a supportive, nurturing, and protective environment. Other research (Fleming, Mullen, & Bammer, 1997) has found several factors associated with a girl's risk of being sexually abused, including experiencing physical abuse; having a mother who is mentally ill; being socially isolated; and not having someone in whom to confide. In addition, whereas an alcoholic father was found to be a risk factor for childhood sexual abuse by a family member, an alcoholic mother was a risk factor for childhood sexual abuse by a person outside the family.

Child molesters are often intoxicated when the abuse occurs. Alcohol's influence on the brain allows a disinhibition of socially proscribed behaviors, including incest and the sexual molestation of children. A 1988 study found 48 percent of fathers who had committed incest were alcoholic but that 63 percent of fathers were drinking at the time of the abuse. However, further research is needed about the extent and nature of the connection between parental AOD and subsequent child abuse.

CHILD ABUSE AS A RISK FACTOR FOR SUBSTANCE ABUSE

A high percentage of drug abusers, particularly those in inpatient and residential treatment programs, report having been sexually abused as children (Dansky, Saladin, Brady, et al., 1995; Moran, Vuchinich, & Hall, 2004; Navajits, Weiss, & Shaw, 1997; Schiff, El-Bassel, Engstrom, et al., 2002; Wallen & Berman, 1992). However, few prospective longitudinal studies have been conducted to determine whether abused and neglected children are more likely to develop AOD problems when they grow up, compared to similar but nonabused children. Of the existing studies, the most consistent finding is that childhood abuse and neglect may increase the risk for alcohol and drug problems, particularly among women. Widom and colleagues followed a large group of children with documented cases of physical and sexual abuse and neglect, and assessed the extent to which they developed alcohol and other drug problems in adulthood. At the approximate age of 29, women (but not men) with documented histories of childhood abuse and/or neglect were at increased risk for alcohol abuse (but not drug abuse) (Widom, Ireland, & Glynn, 1995; Widom, Weiler, & Cottler, 1999). In a further follow-up, abused or neglected women (but not men) remained at risk for alcohol problems (Widom, White, Czaja, et al., 2007), compared to nonabused and non-neglected participants; but at age 40, they also reported the use of illicit drugs (marijuana, cocaine, heroin, and psychedelics) (Widom, Marmorstein, & White, 2006).

In sum, there are a number of ways in which child abuse and drugs may be related. Unfortunately, it is difficult to draw firm policy conclusions from the existing empirical research because of a number of methodological limitations and challenges inherent in research in this area. Ambiguous definitions of child abuse and neglect, varying age ranges defining childhood, varying definitions of alcohol and substance-abuse problems, reliance on retrospective self-reports, use of specialized treatment samples, and lack of control groups threaten the validity and generalizability of findings. Although there is strong justification to expect several levels of association between child abuse and drug abuse, convincing and consistent evidence does not yet exist.

PROPOSED RESPONSES

Reasonable evidence exists to suggest that children who are raised by substance-abusing parents are at increased risk for a number of adversities in childhood, including being abused or neglected; witnessing domestic violence; and being exposed to parents with problems associated with substance abuse (high rates of mental illness, criminal behavior, suicide attempts, etc.). Although more research is needed on the long-term effects of having substance-abusing parents, alcohol and substance-abuse treatment agencies should routinely ask their clients if they have been or are being physically or sexually abused. It is also important that child welfare agencies determine whether caregiver or family member substance abuse is present. In these cases, prevention will depend on advances in the identification and treatment of substance-abusing parents, particularly in primary care settings. The school setting is another primary site for the provision of services to children affected by

parental substance abuse through a variety of programs targeting children of different ages.

Because it is not possible to remove all children from risky family environments, additional research is needed on ways to protect children. Caregivers and professionals can help maltreated children develop coping strategies that do not involve alcohol and/or drugs and help them become more resilient so as to avoid future alcohol and drug abuse. Some children are resilient to negative outcomes, even though they were exposed to drugs in utero or lived with drug-abusing parents. Some of these children might have been sheltered by a caring adult who addressed their needs. The emerging literature on resiliency processes and mechanisms should be reviewed (Rutter, 1990) and used to inform research with children of drug abusers to make preventive interventions more effective.

Children of drug-addicted mothers may be resilient to their high-risk environments if their mothers realize the negative impact of their chaotic lives on their infants and work to improve their parenting skills. Improvement may include finding external supports to learn parenting skills, such as parent-and-family-skills training programs; locating good early childhood education for the child and outside child care; and possibly even considering foster care or adoption. Research has shown more positive outcomes for drug-exposed infants when the mothers were willing to use external social supports when necessary to provide the best opportunities for learning and emotional growth for the child.

See also **Attention Deficit Hyperactivity Disorder; Coping and Drug Use; Families and Drug Use; Fetal Alcohol Syndrome; U.S. Government Agencies: National Institute on Alcohol Abuse and Alcoholism (NIAAA); U.S. Government Agencies: National Institute on Drug Abuse (NIDA).**

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CHILDHOOD BEHAVIOR AND LATER SUBSTANCE USE. A wealth of research has investigated connections between early childhood behavior and later substance use. Studies have examined a range of constructs in isolating predictors of later substance use and misuse. This review provides an overview of key findings and theoretical constructs, including temperamental factors, social learning theory, primary socialization theory, and genetic influences. Although most children and adolescents who experiment with substances do not go on to develop a substance use disorder, most adults with substance use disorders began using substances as youths (Substance Abuse

and Mental Health Services Administration, 2005). Thus, understanding the nature of childhood substance use is crucial to understanding the trajectory toward abuse and dependence.

PERSONALITY FACTORS AFFECTING DRUG USE

Longitudinal personality research has isolated early temperamental predictors of later substance use. Factors of childhood personality have been strongly related to adolescent personality, which is in turn related to adolescent and young adult substance use (Brook et al., 1995). A now-classic study by Jack Block, Jean Block, and Susan Keyes (1988) found personality factors such as poor impulse control, uninhibited emotional expression, and decreased emotional adaptability predicted later marijuana and hard-drug use. Thomas A. Wills and colleagues (2000) showed that high physical activity level, negative emotionality, and inflexibility were risk factors for later substance use. Protective factors against later substance use included the capacity to focus and the ability to experience and express positive emotions (Wills et al., 2000). The environment plays a strong role in the expression and modulation of heritable (capable of being inherited) temperamental traits. For example, life stressors and deviant peer networks have predicted lower impulse control, which increases the risk for later drug use (Wills et al., 2000). Conversely, children who display high levels of impulse control and the capacity to delay reward have demonstrated less vulnerability in response to external stressors (Wills et al., 2000). In summary, certain temperamental traits are predictive of later substance use, but a complex relationship exists between innate traits and the mediating influence of environment in the expression of those traits.

SOCIAL LEARNING THEORY

Social learning theory suggests that parental and peer modeling of substance use influences both the substance-related behaviors of children and children's expectations about the consequences of use. Social learning theory posits three sequential stages of action: (a) observation and imitation, (b) social encouragement and support, and (c) positive expectations toward future substance use (Peratritis et al., 1995). Albert Bandura, the first proponent of social learning theory, emphasized a strong cognitive component, focusing on the shaping of expectancies and pointing out that observation can equip adolescents with the skills either to acquire and use or to reject substances (Peratritis et al., 1995). Accordingly, greater parental use, peer use, and more substance offers have been associated with greater risk of adolescent substance use (Castro et al., 2006; Li et al., 2002). Conversely, parental non-use has demonstrated a buffering effect on the powerful influence of peer use (Li et al., 2002).

PRIMARY SOCIALIZATION THEORY

Primary socialization theory postulates that the socialization process shapes the nature and strength of attitudes and social behaviors, including norms related to drug use. Strong positive affiliations with socialization groups such as families, school systems, and religious groups are more likely to result in the transmission of conventional norms and result in pro-social behavior. Adolescents with higher religiosity have a lower incidence of substance use disorders (Miller et al., 2000), a relationship that extends into adulthood (Kendler et al., 1997). Weak bonds with socialization groups are more likely to result in affiliation with deviant peer clusters, which may ultimately result in deviant behaviors such as substance use (Oetting & Donnermeyer, 1998a). Weak bonds with family are commonly associated with lack of effective parental monitoring, which in turn relates to substance use initiation, escalation, and advancement to abuse (Chilcoat et al., 1996; Reifman et al., 1998; Getz and Bray, 2005). Association with substance-using peers has a well-documented relationship with adolescent experimental substance use (e.g. Petraitis et al., 1995; Getz & Bray, 2005; Mason et al., 2007). Recent work suggests a reciprocal relationship wherein association with substance-using peers directly encourages use, while adolescents who use are more likely to select friends who use substances (Simons-Morton, 2007). Additionally, certain traits such as anger, aggression, and sensation seeking and psychopathologies such as attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder, and antisocial personality disorder interfere with the primary socialization process and make substance use more likely (Oetting et al., 1998b).

GENETIC INFLUENCES

Genetic factors, widely studied in differentiating pathways of substance use, are likely instrumental in the transition from use in childhood to dependency in adulthood (Hasin et al., 2006; Rose & Dick, 2004–2005). Laura Jean Bierut et al. (1998) found genetic risks for substance use disorders to be both common (i.e., one predisposing factor for all substance use disorders) and substance-specific (i.e., distinct genetic factors for alcohol, marijuana, cocaine, and nicotine). Kenneth S. Kendler and colleagues (2003) found only common genetic risks for substance abuse and dependency. A later twin study identified substance-specific factors for both licit and illicit drugs and even further specificity for nicotine and caffeine dependence (Kendler, 2007). Howard J. Edenberg et al. (2004) found a gene that significantly predicts alcohol dependence, a relationship that may be influenced by a neural response to alcohol. Generally speaking, genetic studies have been most conclusive regarding alcohol, demonstrating a heritability of 50–60 percent (Hasin et al., 2006).

CONCLUSION

Early experimental substance use predicts later substance use disorders, and both are related to a variety of intrapersonal, social/contextual, and biological factors. Certain childhood personality traits are associated with adolescent traits, which later relate to experimental substance use. The power of these traits is strengthened or limited through complex environmental interactions. Social learning theory provides a useful framework for understanding how parental and peer modeling of behavior and shaping of expectancies can profoundly influence substance use behavior. Primary socialization theory highlights the important role of social networks in the transmission of behavioral norms about substance use. Naturalistic studies have demonstrated the profound influence parental substance use and quality of child supervision have upon risk for or protection against child substance use. Likewise, having friends who use substances is implicated in both the development and escalation of substance use. While genetic studies have demonstrated a heritable risk for alcohol dependence, it is unclear whether dependence risks are substance-specific or general.

An understanding of these complex and various forces is crucial in more skillfully approaching substance use disorders at the public health level. Current research is focusing on the relative influence of individual variables and their interactions within multi-factorial models. One recent study of a biosocial model, for example, found that intrapersonal influences on substance use behavior become more powerful in more harmful contexts (Foshee et al., 2007). Powerful integrative models provide hope for greater adaptability of research across contexts and effectiveness in translating this work into viable treatment and prevention programs.

See also **Child Abuse and Drugs; Conduct Disorder and Drug Use; Coping and Drug Use; Families and Drug Use; Intimate Partner Violence and Alcohol/Substance Use.**

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CHINA. Ancient China was a golden age for alcohol, although during much of this early period mineral powders were also taken as *immortality drugs*, often in conjunction with wine. The most popular of these substances was called "cold eating powder" (*hanshisan*), used in alchemy with cinnabar and consumed with copious amounts of alcohol between the Latter Han (25 BCE–220 CE) and Tang periods (618–907).

A tea revolution marked the Tang, permanently relegating alcohol to a lesser position among the culturally privileged intoxicants. New processing techniques and advances in cultivation methods combined with the widespread promotion of tea as a suitable substitute for alcohol by monastic Buddhism. Medical writers also acknowledged its medicinal and therapeutic qualities, recommending tea to nurture the stomach, clear inflammations in the throat, and aid digestion.

SPREAD OF SMOKING OPIUM AND TOBACCO

Opium use also appeared during the Tang, and was imported from the Middle East by sea and overland by caravan. By the Ming period (1368–1644), it occupied an important position within traditional medicine and was recommended as a general panacea against a wide variety of ailments, from cholera, plague, heat stroke, headache, inflammations, fever, vomiting, and diarrhea to stomach pains.

At first, however, opium was eaten, and its spread from the eighteenth century onward depended on the discovery of an entirely novel mode of delivery, namely smoking, which began with tobacco. Tobacco was first introduced in China by European traders in the late sixteenth century. The tobacco plant rapidly became a popular crop, particularly in the tropical south where many medicinal virtues were attributed to it. In the hot, humid summers of the south, tobacco fumes were thought useful in fighting off miasmic diseases such as malaria; in the provinces of the north, smoking was used against the effects of cold and hunger.

Opium blended with tobacco, a combination called *madak*, was responsible for the spread of smoked opium. The mixture was prepared by the owners of smoking houses and fetched prices significantly higher than for pure tobacco. Only by the end of the eighteenth century was the tobacco content eliminated, allowing the smoking of pure opium to become a marker of social status: In a period marked by increased social mobility and conspicuous consumption, large amounts of money could be spent in one evening on pure opium. Wealth and status could be displayed far more effectively by smoking many pipes of pure opium than by drinking expensive tea or alcohol.

The shift away from madak toward pure opium was facilitated by changes in the quality of opium produced in India: Malwa—shipped from India by Portuguese traders—not only varied in quality, it was also fiery and irritating when smoked pure, whereas high-quality Patna—produced in India under British control—was mild and pleasant to the palate. The quality of Patna further improved after poppy cultivation in Bengal was monopolized by the East India Company in 1793, the paste being bought and transported to the rest of Asia by independent traders.

THE OPIUM WAR

Between 1797 and 1820 high-quality opium percolated through the coastline in south China following well-established contacts among local merchants, official intermediaries, and contraband traders. Smuggling was undertaken by British, Parsi, Jewish, Dutch, Portuguese, Danish, and American traders as well as local pirates. The sheer amount of illegally imported opium was blamed by some officials for reducing the empire's silver holdings, and a small number of officials in favor of prohibition managed to convince the Daoguang emperor (r. 1820–1850) that war with foreign powers was the only solution. The reasons for the abrupt change in favor of a policy of opium prohibition in the 1830s were also related to internal court politics and not only the consequence of the actions pursued by the British government in support of free trade: Chinese scholars turned opium prohibition into a political agenda, enabling them for the first time since the Manchu conquest in 1644 to challenge the dominant position of the court aristocracy.

As part of a new prohibition policy, the imperial administration dispatched Lin Zexu (1785–1850) in 1839 as commissioner to Guangdong in order to bring all opium imports to a halt. Opium stocks were confiscated, the movement of foreigners was further restricted, and in a highly symbolic act of purification, 20,000 chests of imported opium were burnt in public. The retaliatory action by British forces provided the spark for the first Sino-British War (1839–1842), later remembered as the Opium War. As a consequence of the war, several treaty ports were opened to foreign trade.

POPULARITY OF OPIUM

As the poppy was increasingly cultivated in China, smoking progressed down the social scale during the second half of the nineteenth century and it gradually became a popular marker of male sociability. Either in opium houses or at home, opium would be smoked by friends while enjoying leisurely conversations or in groups where a pipe was passed around. Even among the less privileged, the example of a "lonely smoker" was generally eschewed: Smoking was a collective experience, an occasion for social intercourse, a highly ritualized event including strict parameters for the consumption of opium. During the socioeconomic changes experienced in the second half of the nineteenth century, opium- and teahouses as well as alcohol-serving inns provided spaces of social comfort where even the poor could socialize.

Besides the complex social rituals involved in opium smoking, the medicinal virtues of the paste were a major reason for its spread in the nineteenth century. Opium was primarily a painkiller, and self-medication—before modern synthetic medications

became available—was the chief motive for smoking: to reduce pain, fight fevers, stop diarrhea, and suppress coughs.The lowering of the cost of opium allowed ordinary people to relieve the symptoms of endemic diseases such as dysentery, cholera, and malaria and to cope with fatigue, hunger, and cold. The spread of affordable opium used in small quantities thanks to the sophisticated mechanism of the opium pipe allowed even the most dispossessed to benefit occasionally from the panacea in the nineteenth century.

RISE OF PROHIBITION

If opium was medicine as much as recreation, the transition from a tolerated opium culture to a system of prohibition attempted by China's late imperial and republican governments from 1906 to 1949 produced a cure that was far worse than the disease. After the Boxer Rebellion in 1900 the Qing concluded a number of bilateral treaties, including a commercial treaty with Great Britain in September 1902, an opium treaty with Germany in October 1903, and one regulating the opium trade with Portugal. In 1906 the Qing formally declared a 10-year opium suppression plan with the support of the United States. The foreign powers were so impressed with the achievements during the initial test period that the 10-year agreement was renewed in 1911, the very year that the last dynasty was overthrown: China thus waged the world's first war on drugs, becoming the initial link in a chain of antidrug campaigns that would gradually span the globe in the twentieth century.

Efforts to curb opium use continued in republican China (1911–1949), and a series of opium suppression laws were passed from 1929 to 1934, while the government launched a Six-Year Opium Suppression Plan that not only criminalized the trafficking of illegal drugs but also threatened habitual users who relapsed after treatment with punishments ranging from imprisonment to summary execution. Tens of thousands of ordinary people were imprisoned and died from epidemics in crowded cells, while those deemed beyond any hope of redemption were simply executed. Opium smokers also died in detoxification centers either because the medical authorities failed effectively to treat the ailments for which opium was taken in the first place or because replacement treatments were poorly conceived and badly administered.

MORPHINE AND HEROIN

Official attempts to police the bloodstream of the nation engendered corruption, a black market, and a criminal underclass. They also accelerated the spread of morphine and heroin. Both were widely smoked in the first decades of the twentieth century, although some of the heroin pills taken for recreational purposes contained only a very small proportion of alkaloids and were often based on lactose or caffeine. Morphine and heroin had few concrete drawbacks, and a number of practical advantages that persuaded many opium smokers to switch under prohibition. Pills were convenient to transport, relatively cheap, odorless and thus almost undetectable in police searches, and easy to use because they no longer required the complicated paraphernalia and time-consuming rituals of opium smoking.

Heroin pills, red pills in particular, enabled consumers to replicate the smoking culture created around opium while avoiding most of the problems produced by anti-opium legislation: They allowed narcotic culture to be reproduced in a different legal context. Although some heroin pills were weak in opiate content, semisynthetics were also increasingly injected by the poor. The dirty needles were often shared and sometimes caused lethal septicemia and transmitted a range of infectious diseases.

SUBSTANCE USE UNDER COMMUNISM

The Chinese Communist Party actively participated in the illegal opium trade during its fight against the government in the 1930s and 1940s. Opium was one of the most important financial resources of the party, allowing it to overcome a number of fiscal difficulties and build an alternative state in the hinterland. After the Communist takeover of the country in 1949, however, it took the party a mere three years to eliminate all illegal substances: A dense network of police institutions, resident committees, and mass organizations were used to crush drug offenders, some even being denounced by their own family members. Public trials and mass executions dealt a final blow to the narcotics culture, while tens of thousands of offenders were sent to labor camps, often for life.

Although it is often believed that the Communists successfully eliminated the so-called drug plague, medical and social variables were as important in the long-term erosion of the narcotics

culture as political factors. Penicillin appeared in the 1940s as the first antibiotic that could successfully treat a whole range of diseases that had been managed previously with opium: Antibiotics took over the medical functions of opiates. On the other hand, the social status of opium was already on the decline in the 1930s, abstinence being seen as a mark of pride and a badge of modernity among social elites, very much as the rising middle classes elsewhere started to free themselves from morally reprehensible "drugs."

CIGARETTES

With opium use on the wane, the cigarette was seen as fashionable and modern. Despite the spread of morphine and heroin as alternatives to opium, the commodity that most benefited from prohibition was the ready-made cigarette. It was light and palatable, easy to store and handy to use, capable of delivering nicotine straight to the lungs in short spans of time: perfectly attuned to the faster pace of city life. British American Tobacco thrived in republican China, selling half a billion cigarettes a month in a number of provinces in the 1930s, and under Mao Tse-tung in 1952 its sophisticated system of mass distribution and production was transferred to the authority of the Chinese government.

Tobacco cultivation and cigarette production were vigorously promoted by the Communist Party, as the cigarette was allowed to take over the everyday rituals and social roles of opium within a thriving smoking culture that appeared impervious to the deleterious effects of nicotine. Cigarettes evoked power and prestige, and were promoted by the top leadership. Deng Xiaoping even expressed his gratitude to the cigarette as the reason for his longevity. By the end of the twentieth century China emerged as the largest market for cigarettes and the world's leading tobacco producer. China, for example, produced over 2,000 million kilograms of leaf tobacco in 2000, representing more than a third of the world's production. However, the country is also huge market for foreign leaf tobacco, as over 320 million Chinese are smokers—about a quarter of all smokers around the world. The China National Tobacco Corporation, a government-owned monopoly, annually produces 1.7 trillion cigarettes per year, while those who can afford it prefer to smoke imported cigarettes. The vast majority of China's smokers are male adults, with only 4 to 7 percent women. The tobacco industry contributes about 10 percent of state revenue and has been the state's top revenue generator for over a decade. In the early twenty-first century there are few signs that smoking in China is on the decline.

See also **Britain; Foreign Policy and Drugs, United States; International Drug Supply Systems; Opium: International Overview; Tobacco: An International Overview.**

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CHINESE AMERICANS, ALCOHOL AND DRUG USE AMONG.

According to the 2000 U.S. Census report, the largest subpopulation of Asian and Pacific Islanders (AAPIs) is Chinese American (23%). A total of 2.7 million people reported their ethnicity as Chinese alone or in combination with other Asian groups or races. The Chinese American ethnic community consists of people from many countries: the People's Republic of China, the Republic of China (Taiwan), and various countries in Southeast Asia, Latin America, and the Caribbean. The U.S. Department of Commerce (2004) indicated that 69 percent of Chinese Americans are foreign born, and 83 percent speak a Chinese language/dialect at home.

Given that AAPIs are among the fastest growing minority group in the United States (Chen, 1996) and that Chinese Americans constitute a significant portion of AAPIs, it is important to

understand substance use behavior in the Chinese American population. The discussion that follows presents research evidence for alcohol use, cigarette smoking, and overall substance use among Chinese Americans.

ALCOHOL USE

In China, historically, alcohol was sanctioned for religious ceremonies, especially ancestor worship. Today, in China and among Chinese immigrants, alcohol is commonly served at celebrations and banquets, and some people consume alcohol at meals—beer, wine, brandy, or whiskey. Drinking-centered institutions, however, are absent (Hsu, 1955; Singer, 1972; Wang, 1968). In Chinese tradition, moderate drinking is believed to have medicinal effects, but excessive use is believed to bring on "nine-fold harm" (Yu & Liu, 1986–1987) and is condemned in folk culture as one of the four vices. Examples of the nine-fold harm include impairment of intellect and predisposition to physical illness.

Chinese cultural beliefs regarding the religious and medicinal benefits of moderate drinking and the harm associated with excessive use may control drinking patterns in China, but when people move into a new cultural setting, their alcohol use may be influenced by the extent to which they learn the customs, attitudes, and behavioral characteristics of the surrounding culture. This process is defined as *acculturation* (Austin & Lee, 1989; Zane & Mak, 2003). David Sue (1987) hypothesized that alcohol abuse is more congruent with American, rather than Chinese values, since Chinese values are antithetical to alcohol abuse. Recent research evidence has provided some support for this hypothesis: Acculturation seems to serve as a risk factor for Chinese Americans' drinking behavior (Hahm et al., 2003, 2004; Hendershot et al., 2005, 2008).

Two earlier studies investigated alcohol use among Chinese and other AAPIs. Harry H. L. Kitano and Iris Chi (1986–1987) found differences in alcohol consumption patterns among respondents from Chinese, Japanese, Korean, and Filipino adults. The lowest prevalence of heavy drinking was reported by Chinese Americans (14% male, 0% female). Most of the Chinese male heavy drinkers were in the age category 26–35.

Subsequently, Chi and colleagues (1988) found that among Chinese American males in their Los Angeles sample, those most likely to drink at any level were under the age of 45 and of relatively high social and educational backgrounds. They found that parental drinking, going to or giving parties, and having friends who drank were the important variables distinguishing drinkers from abstainers among their Chinese adult male sample. Furthermore, results of recent research suggested that parental drinking and male gender were significantly associated with a greater likelihood of lifetime and current alcohol use among Chinese and Korean Americans (Hendershot et al., 2005).

Genetic factors that may influence alcohol use among Chinese Americans have been investigated. An ethanol sensitivity, also known as the "flushing syndrome," is caused by deficiency of the aldehyde dehydrogenase isozyme (ALDH2) genotype, which leads to impairment in metabolizing alcohol. Seldom found in whites, ALDH2 deficiency is most commonly observed among people of northeast Asian descent: Chinese, Japanese, and Koreans (Crabb et al., 1995; Wolff, 1973). Possession of ALDH2*2 alleles has been found to be a protective factor against alcohol dependence (Luczak et al., 2006). A group of researchers at University of California, San Diego, have studied extensively the role of ALDH2 in drinking behavior among Chinese American and Korean American college students (Doran et al., 2007; Hendershot et al., 2005; Luczak et al., 2003; Wall et al., 2001). For example, Luczak and colleagues (2003) found that binge drinking (i.e., heavy episodic drinking) was negatively associated with religious service attendance among Korean American college students and Chinese American college students with Western religious affiliation. In addition, this protective effect of religious service attendance was stronger among those who were not protected by an ALDH2*2 allele.

CIGARETTE SMOKING

Smoking among Chinese Americans is a serious public health problem (Hu et al., 2006). Although Chinese Americans seem to smoke less than whites and other AAPIs (Price et al., 2002), smoking prevalence within the Chinese American population is high. The smoking prevalence among men has been significantly higher than that among women (Centers for Disease Control, 1992; Fu et al., 2003; Thridandam et al., 1998). In the first population-based study of

Chinese Americans' smoking behavior, Yu and colleagues (2002) found that the prevalence of smoking was 2 percent for females and 34 percent for males. Particularly, male prevalence of smoking is far above the Healthy People 2010 target goal, initiated by the U.S. Department of Health and Human Services.

In addition to gender, research evidence has suggested that the prevalence of smoking among Chinese Americans varies depending on a number of factors including English proficiency, healthcare utilization, cultural beliefs, and education level. Yu and associates (2002) found that low education level was significantly associated with smoking among men. This relationship is consistent with research findings in China (Chen, 1995).

In terms of healthcare utilization, Yu and colleagues (2002) found that smoking among men was significantly linked to utilization of non-Western healthcare resources and lack of knowledge of early cancer warning signs. Similarly, in a sample of Chinese American males, Kent K. Hu and colleagues (2006) found that current smokers had less knowledge about the health effects of tobacco compared to non-smokers. Compared to former smokers, current smokers were less likely to have a regular doctor.

In terms of English proficiency, Hu and colleagues (2006) found that current smokers were less likely to be proficient in English than those who had never smoked. Yu and colleagues (2002) suggested that English proficiency may be a factor that is closely linked to age. Men with lower English proficiency tended to be older and foreign-born and reported significantly higher rates of current smoking compared to a sample of younger participants with higher English proficiency, which reported lower rates of current smoking. In addition, researchers (Fu et al., 2003) found that less English-proficient Chinese American male smokers are not as likely to receive advice on quitting smoking from a physician.

Cultural beliefs related to cigarette smoking have played an important role in Chinese Americans' smoking behavior (Hu et al., 2006; Tu et al., 2000). In Shin-Ping Tu and colleagues' study (2000), they found several culturally bound themes for cigarette use and smoking cessation. For instance, based on the concept of *yin* and *yang*, some participants believed that physical exercise may "balance" the negative consequences of cigarettes. Individuals also reported that smoking is a culturally accepted behavior, such that refusing to accept cigarettes offered in social situations is perceived as impolite and disrespectful. In Hu and colleagues' study (2006), they found that male smokers were more likely to have these traditional cultural beliefs about smoking than non-smoking males. Overall, the researchers suggested that these traditional beliefs, which indicated more favorable attitudes toward smoking, may pose challenges for smoking cessation among Chinese American men.

Recent research has also examined the link between depression and smoking among the Chinese American population. Janice Y. Tsoh and associates (2003) found that the level of depressive symptoms among Chinese American smokers is analogous to those observed in white populations in the United States. Higher levels of depressive symptoms were more common among female participants and those who were not employed. These symptoms were also associated with significant nicotine withdrawal and high temptation to smoke when experiencing negative emotional situations.

Given the important role of culture in smoking behavior, culturally appropriate smoking cessation programs have been developed for both Chinese American youth and adults (Fang et al., 2006; Ma et al., 2004). Both studies achieved positive results. Particularly, 38 percent of adult smokers (Chinese and Korean Americans) reported quitting smoking three months after receiving intervention in Fang and colleagues' study. The results of these studies provide promising steps toward developing efficacious smoking cessation programs for Chinese Americans.

OVERALL SUBSTANCE USE

Increased efforts have been made to examine the within-group difference in substance use behavior among AAPIs. Based on two earlier studies in San Francisco, Tooru Nemoto and colleagues (1993, 1999) found that drug use patterns vary depending upon ethnicity, gender, immigrant status, and age group. For example, compared to other Asian ethnic groups, Chinese Americans were more likely to take sedatives orally and less likely to inject drugs. Most Chinese Americans used marijuana as their

first illicit drug, and social pressure from friends was noted as the most common reason to begin using drugs. The Chinese immigrants did not begin using drugs until immigrating to the United States. This may be due to low accessibility of illicit drugs in their native country.

Studies based on large samples of AAPI youth in Hawaii and California have consistently reported that Chinese American adolescents have the lowest rates of substance use compared to white, Filipino, Japanese, and Pacific Islander/Hawaiian adolescents (Pearson, 2002; Wong et al., 2004). In a California statewide sample of 4,300 Asian American high school students, Teresa A. Otsuki (2003) found that for Chinese American females, alcohol, marijuana, and cigarette use were significantly related to depression. Smoking had an inverse relationship with self-esteem.

Rumi Kato Price and colleagues (2002) examined data from large national surveys and found that rates of substance use and abuse among Chinese Americans were significantly lower than Japanese Americans. For example, Chinese American adults had significantly lower rates of any alcohol use and cigarette smoking in a 12-month period than those of Japanese American adults. Chinese American youth had significantly lower rates of any alcohol use and cigarette smoking in a 12-month period than those of Japanese American youth. Authors also noted higher rates of smoking and drinking among Korean American youth than those among Chinese American youth. In addition, researchers found that mixed-heritage Chinese American youth were 4.3 times as likely to use substances as those who had unmixed-heritage. The results of this study highlighted the potential need for reclassifying ethnicity to estimate substance use and abuse among Chinese American adolescents.

In a study to examine etiology and prevention of substance use among AAPI youth, Tracy W. Harachi and colleagues (2001) reviewed three studies and indicated several factors related to substance use among Chinese American youth. For example, parents' and peers' disapproval for substance use were negatively related to lifetime use of cigarettes, alcohol, and marijuana. Family discord and greater level of acculturation were positively related to alcohol use. Harachi et al. (2001) recommended that more research is needed to examine risk factors for substance use among Chinese Americans and other AAPIs.

GOALS FOR TWENTY-FIRST-CENTURY RESEARCH

In earlier studies, much of the research on substance use was based on grouping all AAPIs together. Researchers made significant efforts in examining the ethnic difference in substance use among AAPIs from the 1990s to the early twenty-first century. This step enabled them to compare substance use patterns between Chinese Americans and other ethnicities. Although Chinese Americans overall exhibit lower rates for alcohol and other drug use, smoking remains a serious health issue for Chinese Americans (Hu et al., 2006). While research evidence has indicated a few important social, environmental, and cognitive factors that influence substance use among Chinese Americans, more research is still needed to enhance the understanding of smoking behavior among Chinese Americans.

See also **Risk Factors for Substance Use, Abuse, and Dependence: Race/Ethnicity.**

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CHLORAL HYDRATE. Chloral hydrate is one of the oldest sedative agents still in use. It was made by the German chemist Liebig in 1832 and introduced into general use in 1869 as a substitute for laudanum, an alcoholic solution of opium. Chloral hydrate differs from the barbiturates in that it is a simple molecule composed of two carbon atoms, three hydrogen atoms, two oxygen atoms, and three chloride atoms. It is the famous (or infamous) substance added to alcohol to make a *Mickey Finn*, a drink known to cause those who drink it to become unconscious. Because it shares many effects of other central nervous system depressants, it can be used to treat the alcohol withdrawal syndrome. Chloral hydrate was a popular sedative for elderly patients because its effects occur quickly, last only a short time, and leave no nagging hangover effect. However, it is inconvenient to use (up to 2 grams must be taken by mouth) and, after the introduction of the benzodiazepines, its use has decreased.

See also **Benzodiazepines; Opiates/Opioids; Sedative.**

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CHLORDIAZEPOXIDE. Chlordiazepoxide (brand name Librium) is a member of the benzodiazepine family of drugs currently used to treat insomnia, anxiety, muscle spasms, and some forms of epilepsy. It was the first benzodiazepine to be used in clinical practice in the 1960s, as an alternative to phenobarbital or meprobamate, in treating psychoneuroses, anxiety, and tension. Its advantage over barbiturates and other central nervous system depressants is that it is less toxic, especially after an overdose.

In addition to the previously mentioned uses, chlordiazepoxide is frequently used to treat the seizures or delirium tremens (DTs) that appear during alcohol withdrawal. In the late 1990s, Dr. Michael Mayo-Smith conducted a meta-analysis to determine if benzodiazepines effectively prevent delirium in patients experiencing DTs. Although benzodiazepines were shown to be effective, this study was not conclusive since chlordiazepoxide was the only benzodiazepine tested, and further testing is needed on other benzodiazepines before an overall claim can be made (Johnson et al., 1997).

See also **Barbiturates; Benzodiazepines; Delirium Tremens (DTs); Meprobamate; Phenobarbital.**

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Revised by publisher (2001)

CHOCOLATE. An ingredient of many popular treats—candies, sweets, baked goods, soft drinks, hot drinks, ice cream, and other frozen desserts. It is prepared, often as a paste, from the roasted crushed seeds (called cocoa beans) of the small South American cacao tree called *Theobroma cacao* (this is not the shrub known as the coca plant, which produces cocaine, *Erythroxylon coca*).

The cacao tree has small yellowish flowers, followed by fleshy yellow pods with many seeds. The dried, partly fermented fatty seeds are used to make the paste, which is mixed with sugar to produce the chocolate flavor loved throughout the world. Cocoa butter and cocoa powder are other important extracts from the bean. Cocoa beans were introduced to Europe by the Spanish, who brought them back from the New World in the sixteenth century. They had first been used by the civilizations of the New World—Mexicans, Aztecs, and Mayan royalty—in a ceremonial unsweetened drink and as a spice in special festive foods, such as molé. They were first used in Europe by the privileged classes to create a hot, sweet drink. By the seventeenth century, cocoa shops and coffee shops (cafés) became part of European life, serving free tobacco with drinks and thereby increasing trade with the New World colonies.

Chocolate produces a mild stimulating effect caused by the theobromine and caffeine it contains. Both are alkaloids of the chemical class called xanthines. Theobromine in high doses has many effects on the body, and it is possible to become addicted to some xanthines, such as caffeine. Nevertheless, some people are so attracted to the flavor that compulsive or obsessive use has resulted in the newly coined term *chocoholic*. Some scientists are researching the phenylethylamine in chocolate as the factor that encourages compulsive chocolate ingestion.

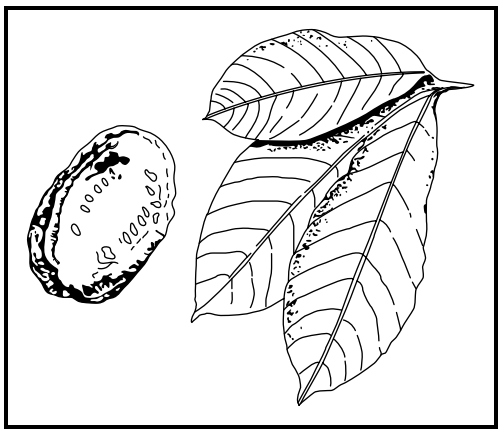

Figure 1. Cacao leaves and pod. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Alkaloids; Caffeine; Theobromine.**

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CHROMOSOME. Chromosomes are structures in the nucleus of the cell that contain the DNA or hereditary material which form genes. Genes are the commonly known units of heredity, and some may contribute to a tendency toward addiction in ways that are not yet understood. Each chromosome is an elongated structure that is clearly visible during cell division. Humans possess twenty-three pairs including the sex chromosomes. A male has an X and a Y sex chromosome, whereas a female has two X sex chromosomes. One of each pair comes from each parent.

See also **Gene.**

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CHRONIC PAIN. Chronic or persistent pain is defined as pain that lasts for longer than six months. Chronic pain can stem from cancer, illness, injury, or postsurgical changes. Often, persons with chronic pain suffer from syndromes that cannot be confirmed

by laboratory tests. These chronic pain syndromes include central pain syndromes, fibromyalgia, headache, lower back pain, myofascial pain syndrome, neuropathic pain, and phantom limb pain. Frequent locations of chronic pain include the back, head, joints, chest, abdomen, and extremities. Chronic pain is common and its sufferers are more likely to have anxiety or depression, have poor perception of their health, decreases in their quality of life, and experience a disruption of their livelihood than those who are not in pain.

In most cases, there is no cure for the chronic pain so treatment is aimed at pain control and rehabilitation. Unfortunately, chronic pain is often ineffectively treated because physicians can be reluctant to prescribe strong, potentially addictive medications. The ineffective pain treatment is compounded by commonly associated conditions such as depression, insomnia, fatigue, and a decrease in general physical functioning. Therefore, treating the pain alone is not sufficient.

The optimal approach to the chronic pain sufferer is an interdisciplinary team that may be comprised of a pain management physician, nurse specialist, psychologist, physical therapist, pharmacist, and vocational counsellor. The physician conducts a thorough assessment of the patient and determines the appropriate medical interventions. The psychologist conducts a thorough psychological assessment, educates the patient on techniques to reduce pain, and tends to any associated mental health illnesses. The nurse specialist acts as a case manager and educator. The physical therapist ascertains the patient's physical endurance, flexibility, and strength and conducts the physical rehabilitation process. The vocational counsellor identifies and devises strategies to allow the patient to return to work. In addition to dispensing medications, the pharmacist will review past and present use of medicinal agents and educate the patient on the proper use of medications.

PHARMACOLOGICAL MANAGEMENT OF CHRONIC PAIN

In the treatment of chronic pain, drugs (analgesics) are usually administered in a stepwise fashion beginning with mild, relatively safe agents and progressing to stronger agents as necessary. In 1986, the World Health Organization (WHO) proposed a stepwise plan, frequently called the analgesic ladder, for the oral treatment of cancer pain. This plan provides adequate pain relief for up to 90 percent of cancer patients but may have limited success for other chronic pain patients. Step one of the ladder is recommended for patients with mild pain and consists of nonopioid analgesics, step two is for moderate pain and consists of mild opioids, and step three is for severe pain and consists of strong opioids. More than one analgesic may be used at a time for an added effect, a procedure called adjuvant therapy.

Nonopioid analgesics consist of acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). Acetaminophen is an effective analgesic that has a minimal side effect profile. Nonsteroidal anti-inflammatory drugs have both analgesic and anti-inflammatory properties. Examples of nonsteroidal anti-inflammatory drugs are aspirin, ibuprofen, naproxen, meclofenamate, piroxicam, and more recently celebrex and vioxx. Major side effects associated with the use of nonsteroidal anti-inflammatory drugs include kidney toxicity, bleeding disorders, and stomach disorders.

Opioid analgesics are available in different strengths. Examples of opioid analgesics are morphine, fentanyl, methadone, and meperidine. The side effects of opioids may be much more serious than those seen with nonopioid analgesics. Side effects include respiratory depression, alterations in consciousness (e.g. drowsiness, sedation, confusion), nausea, vomiting, constipation, urinary retention, and itching.

Other medications used in the treatment of chronic pain include antidepressants and anticonvulsants. Nerve blocks, injection of anesthetics into trigger points, or injection of steroids into the epidural space of the spinal cord may also be utilized. Implantable methods are utilized as treatments of last resort. These methods involve implanting drug delivery systems or electrodes into specific areas of the spinal cord.

TOLERANCE, DEPENDENCE, AND ADDICTION

The continued use of opioids leads to tolerance, in which increasingly higher doses of drug must be used to obtain the original level of pain relief. Tolerance develops slowly, occurring over a period of months to years. Cross-tolerance to other opioids develops, although to a lesser extent. Tolerance can be differentiated from physical dependence and addiction.

Physical dependence is a characteristic of opioid use because of the mode of action. It reflects a state of neurological adaptation to the drug. With physical dependency, discontinuation of opioid use leads to withdrawal symptoms (e.g. sweating, tearing, rapid heart rate, nasal discharge, abdominal cramps, nausea, and vomiting). To prevent withdrawal symptoms, patients on long term opioid use are gradually weaned off the medication. Physical dependence on opioids does not lead to addiction, although it may compel the patient to seek opioids to relieve symptoms of withdrawal.

For chronic pain patients taking opioids, tolerance and physical dependence are not indicators of addiction. Addiction is not a characteristic of opioid use, rather, it is dependent upon the user. In fact, the medical use of opioids is only very rarely associated with addiction. The agonist-antagonist class of opioids (buprenorphine, butorphanol, nalbuphine, pentazocine, and dezocine) has a low abuse potential.

Any patient taking opioids to treat chronic pain can meet the criteria for addiction set forth by the American Psychiatric Association in the *Diagnostic and statistical manual of mental disorders: DSM-IV*. Therefore, it is very difficult to diagnose addiction in chronic pain patients who are taking opioids. Chronic pain patients who are being ineffectively treated could display the drug-seeking behavior that is characteristic of addiction, a phenomenon called *pseudoaddiction*. Alternatively, the patient receiving effective pain treatment may take extreme measures to insure an adequate supply of medication. This behavior is termed *therapeutic dependence*.

Suggestive signs of addiction within the context of opioid therapy for chronic pain include:

- Loss of control over opioid use;
- Preoccupation with the use of opioids despite adequate pain control; and
- Continued use of opioids even with their adverse consequences.

See also **Analgesic; Opiates/Opioids.**

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CIVIL COMMITMENT. The term used for compulsory or mandatory drug abuse treatment is *civil commitment*. Civil commitment is a community alternative to prison that can include temporary court-ordered treatment confinement for chronic drug abusers, particularly narcotic addicts responsible for a large number of crimes. Civil commitment is a strategy for diverting drug abusers, who would not seek treatment voluntarily. In early studies civil commitment decreased daily narcotic use and criminal involvement and in later studies had similar outcomes to voluntary community treatment (Leukefeld & Tims, 1988; Leukefeld, Tims & Farabee, 2002).

Currently the criminal justice system is crowded with drug abusers. For example, more than 700,000 U.S. prisoners have re-entered the community every year since 2000 (Glaze & Bonczar, 2006). A high number of these prisoners are drug abusers. For example, 83 percent of state prisoners reported drug use, and 32 percent reported drug use at the time of their offense (Mumola & Karberg, 2006). About half of jail inmates meet dependence criteria (Karberg & James, 2005), and two-thirds of arrestees in major U.S. cities drug tested positive (NIJ, 2003). Almost 70 percent of probationers reported using drugs or alcohol (Mumola, 1998; Leukefeld, Tims, & Farabee, 2002).

Since the early 1980s the justice system has focused on determinate sentencing and long prison terms, which increase the number of incarcerated drug abusers. Prison-based treatment improves outcomes (Prendergast, Hall, Wexler, Melnick, & Cao, 2004; Wexler, 2003) as does aftercare and continued care (Inciardi, Surratt, Martin, & Hopper,

2002; McCollister, French, Inciardi, Butzin, Martin, & Hopper, 2003), which are similar to civil commitment but cost less. In addition, the popularity of prison diversion in an increasing number of drug courts (Belenko, 2001; Wilson, Mitchell, & Mackenzie, 2006) is, like civil commitment, a way of keeping drug users in the community rather than in prison.

HISTORICAL CONTEXT

The first United States compulsory treatment facility was established in 1935 as the U.S. Public Health Service Hospital for the treatment of narcotic addicts in Lexington, Kentucky, and was called a *farm* then. Three years later, a second hospital was established in Fort Worth, Texas, to provide treatment after detoxification. Early follow-up studies in the 1940s reported that narcotic addicts treated under legal coercion with post-hospital supervision had better outcomes than voluntary patients (Maddux, 1988). However, later studies did not generally support these early positive findings. Consequently, federal treatment staff recommended the enactment of a federal civil commitment law for narcotic addicts.

In 1962 President John F. Kennedy convened the White House Conference on Narcotic and Drug Abuse, which recommended that a federal civil commitment program for narcotic addicts be developed to treat narcotic addicts—mostly heroin addicts. Civil commitment was advocated to protect society by reducing crime and to rehabilitate drug abusers; this resulted in the federal Narcotic Addict Rehabilitation Act (NARA) of 1966. At that time almost twenty-five states had their own civil commitment laws (Inciardi, 1988). For example, California began the first civil commitment program, called the Civil Addict Program (CAP). Because of its relative success, the New York Narcotic Addiction Control Commission (NACC) established the largest and costliest civil commitment program in 1966, called the New York State Civil Commitment Program.

BACKGROUND

In 1962 the U.S. Supreme Court upheld the case of *Robinson v. California* (370 U.S. 660) and ruled that a state could establish a program of compulsory treatment or civil commitment for narcotic addiction and that such treatment could involve periods of involuntary confinement, with penal sanctions for failure to comply. Consequently, the California Civil Addict Program (CAP) was initiated with clear correctional department commitment procedures. Narcotic addicts convicted of a felony or misdemeanor were committed for seven years and then returned to court for disposition of their original charge, or their time served was credited toward their sentence. Addiction was determined by two court-appointed physicians, and patients underwent a sixty-day evaluation period (McGlothlin, Anglin, & Wilson, 1977). Both inpatient and outpatient phases were used for treatment, which incorporated modified therapeutic community principles. During the 1970s infrequent drug use was tolerated by the California Civil Commitment Program if the narcotic addict's overall behavioral pattern was acceptable (Anglin, 1988). This resulted in an overall finding that participants exhibited sustained reductions in drug use, fewer multiple relapses, and relapses that were of shorter duration separated by longer periods of non addiction (Anglin, 1988). However, by 1990, the length of the California commitment period was reduced from seven years to about three years, the community treatment phase was less organized, ancillary services were dramatically cut, and no treatment service was available beyond a minimal, 120-hour Civil Commitment Education Program (Wexler, 1990).

ALTERNATE TO INCARCERATION

The federal NARA, the California CAP, and the New York civil commitment programs were developed to control and to rehabilitate compulsive drug abusers by providing treatment as an alternative to incarceration in correctional facilities. Eligible addicts convicted of a crime could be committed by the court or could choose commitment rather than incarceration. Narcotic addicts not involved in criminal proceedings could commit themselves voluntarily or could be involuntarily institutionalized with a petition from another individual (McGlothlin, Anglin, & Wilson, 1977). Supervised aftercare with drug testing was a major part of civil commitment, which ranged from three years to seven years. Although most studies reported that federal civil commitment was generally not successful, the federal funding for community follow-up treatment in the NARA

legislation provided seed money for establishing drug-treatment programs in major U.S. urban areas (Maddux, 1988). Although the New York State Civil Commitment Program failed (Inciardi, 1988), which was partly attributable to its administration by a social welfare agency with little experience with narcotic addicts, the California program was moderately effective in modifying behavior by using experienced and trained addictions treatment personnel (Anglin, 1988). Specifically, California follow-up studies found that participants reduced their daily heroin use as well as their property crime and antisocial activities. Although many became re-addicted, their relapses were typically shorter and less frequent than individuals not involved in civil commitment treatment (Anglin, 1988). The general conclusion drawn from these studies was that civil commitment, when adequately implemented, might be effective in reducing narcotic addiction. However, repeated interventions were typically required because drug dependence is a chronic condition marked by relapses (Leukefeld & Tims, 1988) or as commonly depicted in the early twenty-first century—drug addiction is a chronic and relapsing disorder.

EVALUATION OF CIVIL COMMITMENT

Civil commitment helped narcotic addicts enter treatment and proved successful for some. Outcome studies generally show that successful treatment is associated with the amount of time spent in treatment and that long-term community supervision with drug testing is important for compulsory treatment. In addition, civil commitment can make treatment available before a crime is committed, and it provides clear treatment goals rather than only punishment. However, civil commitment has limitations. It is costly and can overwhelm facilities without adequate funding and staff. Many addicts are also unwilling or unsuited for participation. Although external coercion such as civil commitment can bring drug users into treatment, it cannot assure that drug abusers will be motivated to engage in treatment. Finally, civil commitment is controversial, because it restricts an individual's constitutional rights of free choice.

See also **Civil Remedies; Coerced Treatment for Substance Offenders; Conduct Disorder and Drug Use; Criminal Justice System, Treatment in the; Drug Courts; Drug Interdiction; Narcotic Addict Rehabilitation Act (NARA); New York State Civil Commitment Program; Prisons and Jails; Prisons and Jails, Drug Treatment in; Rockefeller Drug Laws; Treatment, Specialty Approaches to: Therapeutic Communities; Treatment, Stages/Phases of: Aftercare; Treatment Accountability for Safer Communities (TASC); Treatment: Outpatient versus Inpatient Setting; U.S. Government Agencies: U.S. Public Health Service Hospitals.**

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CIVIL REMEDIES. Civil remedies are defined as procedures and sanctions, specified by civil statutes and regulations, used to prevent or reduce criminal problems and incivilities (Mazerolle & Roehl, 1998). Drug control is a primary application of many civil remedy programs. Police departments, city prosecutors, and community members use civil remedies in an effort to disrupt illegal activities at drug-selling locations. This approach to drug control typically targets non-offending third parties (e.g., landlords, property owners) and utilizes nuisance and drug abatement statutes. These types of abatement statutes include repair requirements, fines, padlocks/closing, and property forfeiture and seek to make owners and landlords maintain drug- and nuisance-free properties. Police often work with teams of city agency representatives to inspect drug nuisance properties, coerce landowners to clean up blighted properties, post "no trespassing" signs, enforce civil law codes and municipal regulatory rules, and initiate court proceedings against property owners who fail to comply with civil law citations.

Growth in the use of civil remedies as a crime control or crime prevention tactic is attributable to several factors. First, the accessibility of civil remedy tools provides frustrated and disadvantaged communities with alternative avenues to reverse the spiral of decline. Second, the increasing use of civil remedies comes at a time when communities and law enforcement officials recognize that many criminal remedies are neither effective nor desirable for a wide range of problems. Third, growth in civil remedy approaches to crime control coincides with increasing societal emphasis on prevention.

Many civil remedy actions seek to reduce signs of physical (e.g., broken windows, graffiti, trash) and social (e.g., public drinking, loitering, public urination) incivilities in the hope that cleaned-up places will break the cycle of neighborhood decline and subsequently decrease victimization, fear of crime, and alienation. Code enforcement, drug nuisance abatement, neighborhood cleanup and beautification, and Crime Prevention through Environmental Design (CPTED) interventions are civil remedy actions that are typically used to control drug problems. Youth curfews, gang injunctions, ordinances controlling public behavior, and restraining orders are other examples of civil remedies that seek to alter criminal opportunities and prevent drug-selling problems from escalating.

Pressures on property owners and managers often result in corrections of health and safety violations, enforced cleanup and upkeep efforts, evictions of problem tenants, and improved property management. Bans on drug paraphernalia, alcohol-related billboard advertising, spray paint, and cigarette machines in high crime areas are used in an attempt to disrupt the illegal activities at drug-selling locations. Injunctions against gangs, youth curfews, and domestic violence restraining orders are used to prevent and deter potential perpetrators

from engaging in criminal behavior. When useful civil statutes are absent, community groups, legislators, and policy makers often work together to enact new legislation.

Unlike traditional criminal sanctions, civil remedies attempt to resolve underlying problems (e.g., the motel's poor management, the absentee owner's neglect). The use of civil remedies tends to be proactive and oriented toward prevention; it aims to enhance quality of life and eliminate opportunities for problems to occur or reappear.

Police use existing public health and controlled substances acts to send warning letters to property owners informing them that complaints of problem activities (e.g., drug dealing) have been reported on their property, advise them of steps to take in preventing or minimizing the problems, and offer assistance in resolving the problem. The letters serve as an official notice of drug activity. Fines and other civil penalties may occur if violations are not corrected, and there are fees for reinspections to cover city costs. If owners do not correct the problem, there are penalties that include fines, closure of the property for up to one year, and sale of the property to satisfy city costs. The city attorney's office can file suit against owners who do not take responsibility for their property.

Civil remedies offer an attractive alternative to criminal remedies since they are relatively inexpensive and easy to implement. Citizens can make a difference by documenting problems, urging police and prosecutors to take appropriate civil action, or spearheading drives to establish useful local ordinances. A group of neighbors can pursue a nuisance abatement action in small claims court without the assistance of police or public prosecutors (Roehl, Wong, & Andrews, 1997). Moreover, civil laws require a lower burden of proof than criminal actions and do not involve the requirements of criminal due process, making them easier to apply yet open to concerns about fairness and equity (Cheh, 1991).

A nonprofit organization, Safe Streets Now! (SSN), has developed a civil remedies program that is based on filing small claims court actions against property owners who fail to address known problems on their property. However, in the thirty-five programs around the United States that have adopted this approach as of 2008, the vast majority of problems are corrected before the filing of a court action. The program seeks to empower neighborhood groups and enhance community organizing. In a 2000 study the SSN approach was lauded as an excellent one for reducing or eliminating issues with problem properties. However, the study also revealed that successful programs were dependent on effective program directors.

The use of civil remedies to solve crime and disorder problems continues to grow in popularity. Police regularly use civil laws, local city regulations, and ordinances to control drug, disorder, and other crime problems. Community groups often work with policy makers to instigate civil remedy action to solve intractable neighborhood problems. The civil remedy approach appears to be an effective and relatively cost-effective approach to control drug problems (Mazerolle, Price, & Roehl, 2000).

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CLINICAL TRIALS NETWORK. The National Institute on Drug Abuse (NIDA) established the National Drug Abuse Treatment Clinical Trials Network (CTN) to accelerate the translation

of science-based addiction treatments into community-based practice.

The mission of the CTN is to improve the quality of addiction treatment throughout the nation, using science as the vehicle. The network brings together practitioners from community-based drug abuse treatment programs and scientists from university-based research centers in an alliance that fosters communication and collaboration. This alliance facilitates the development and implementation of evidence-based treatments in community practice settings. Two key principles guide the activities of the CTN:

1. Addiction treatment services will improve as evidence-based treatments are broadly implemented in community-based treatment programs.
2. Randomized controlled clinical trials are the gold standard for generating evidence-based treatments.

The CTN has completed more than 20 clinical trials and enrolled more than 9,000 trial participants. These trials have tested pharmacological, behavioral, and integrated treatment interventions for adolescents and adults with a variety of substance use disorders. Some of the CTN's findings have been packaged into comprehensive training and treatment tools for use by practitioners.

INFRASTRUCTURE AND PROCESS

The CTN actively engages community practitioners in the research enterprise through a formal infrastructure. The network started in 1999 with six university-based research centers and about 40 community treatment programs. It is now a collaboration of 16 research centers and more than 150 treatment programs working cooperatively with NIDA. Scientists and practitioners from a variety of medical and behavioral treatment specialties are represented. CTN researchers are internationally prominent experts in substance abuse, and many of the network's treatment programs are acknowledged as leading programs in patient care. A clinical coordinating center (CCC) and a data and statistics center (DSC) provide research operations and advisory support. By-laws guide the CTN and stipulate that researchers and practitioners have equal influence in the network's activities. NIDA administers the CTN's affairs through its Center for the Clinical Trials Network (CCTN).

The CTN infrastructure provides the foundation for sound planning and ensures the quality, reliability, and utility of the results of its research. The policies and procedures of the CTN support the mission and infrastructure, guide the research, and ensure process integrity. The following steps in the research life cycle outline this approach:

1. In consultation with NIDA, CTN researchers and practitioners propose and select research topics and identify a research team to lead each study.
2. An independent review board (Data and Safety Monitoring Board) initially and periodically assesses each research study for its public health significance, scientific integrity, and design adequacy, as well as participant safety and ethical considerations.
3. Compliance with federal regulations for research conduct and human subjects protection is required. It includes those protections required by the Office for Human Research Protections (OHRP, http://www.hhs.gov/ohrp/), the Food and Drug Administration (FDA, http://www.fda.gov/), and local institutional review boards.
4. The DSC and CCC monitor data management, protocol adherence, and regulatory compliance.
5. The NIDA CCTN oversees investigator performance and trial progress.

ACCOMPLISHMENTS AND FUTURE DIRECTIONS

The primary focus of the CTN's first 20 clinical trials has been to test pharmacological, behavioral, and integrated treatment approaches for substance use disorders. CTN trials have also addressed topics ranging from the treatment of substance use disorders in special patient populations, including adolescents, pregnant women, patients with co-occurring mental health disorders, and Spanish speakers, to the integration into substance abuse treatment programs of interventions aimed at the prevention of infection with HIV and sexually transmitted diseases. In addition to these large multisite

clinical trials, more than 30 smaller studies have used the CTN infrastructure to investigate the cost-effectiveness of treatment interventions, pharmacogenetics, drug use epidemics in underserved populations, and many other issues. The network's diverse research activities have been and will continue to be a fertile training ground for university- and community-based clinician-investigators and research staff, including international research fellows. For more details on the CTN program and specific CTN research studies, see the network's Web site at http://www.drugabuse.gov/CTN/.

The CTN has engaged in the following dissemination initiatives to ensure that its research results are widely accessible and that its findings are efficiently communicated to treatment providers:

- NIDA has joined with the Substance Abuse and Mental Health Services Administration (SAMHSA) to form the Blending Initiative (http://www.drugabuse.gov/), which seeks to make evidence-based addiction treatments available and readily accessible. Through this mechanism, findings from CTN studies are incorporated into tools that treatment providers can use in their practices.
- The CTN's Dissemination Library (http://ctndisseminationlibrary.org/) is the public repository of its scientific publications, treatment manuals, presentations, study brochures, and other materials.
- Data sets (http://www.ctndatashare.org/) for completed CTN trials are made available to the public to permit the wider research community to use the data and derive the greatest possible benefit from the network's resources.

The CTN's position at the intersection of the research and clinical provider communities will continue to allow the network to address urgent challenges in drug abuse treatment. Areas for future study may include the integration of primary care and substance abuse treatment systems, the development and delivery of effective chronic care models for addiction treatment, and the assessment of holistic approaches to the treatment of patients with co-occurring substance use and mental health and somatic disorders.

See also **U.S. Government Agencies: National Institute on Drug Abuse (NIDA); U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA).**

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BETTY TAI

CLONE, CLONING.

Cloning has multiple definitions in the scientific world. In molecular biology, *cloning* refers to the isolation or amplification of an exact replica of a DNA sequence. DNA clones are typically manipulated by making small code changes and/or splicing multiple pieces together prior to use in experiments. Cell clones are exact copies of individual cells and are typically used for experiments that involve multiple replications under different conditions or for producing mass quantities of a cellular product. Animal clones are derived from a single cell and are genetically identical to the donor animal.

Cloning is an essential technique in drug addiction research, particularly in the generation of genetically engineered mice. In the early twenty-first century mice were becoming the organism of choice for drug addiction research because their neural circuitry and neurochemistry are similar to humans, and they readily partake in and respond to drugs of abuse. Moreover, the ability to remove or overproduce single genes in mice allows researchers to study the influence of particular genes on the neurochemical and behavioral effects of addictive drugs. To genetically engineer mice, the DNA of stem cells is altered in the laboratory using molecular cloning. These manipulated cells are then used to create two lines of mice that are genetically identical with the exception of a single gene; one

line possesses a normal copy of the gene, whereas the other line has a mutated copy. By comparing the drug-induced changes in the brains and behavior of the two mouse lines, researchers have been able to selectively assess the contribution of single genes to drug addiction.

One example of the use of cloning in drug addiction research is the generation and characterization of dopamine transporter (DAT) knockout mice. The DAT gene was of great interest because it codes for the protein that clears dopamine from the synapse and is a target for cocaine. The blockade of DAT by cocaine and the resulting increase in synaptic dopamine is thought to underlie many of cocaine's euphoric and addictive properties. Embryonic stem (ES) cells derived from a normal mouse were amplified using cellular cloning, meaning that scientists started with a few ES cells and let them divide over multiple generations to produce millions of identical clones. Then, molecular cloning techniques were used to delete essential DNA sequences specifically in the section of the genome that codes for the DAT. These altered ES cells were used to generate mice that are identical to normal mice except for their inability to produce any DAT. By characterizing the neurochemistry and behavior of these mice at baseline and following cocaine administration, scientists have learned a great deal about the DAT-dependent and DAT-independent effects of cocaine and their relationship to drug addiction, as well as other behaviors mediated by dopamine.

See also **Dopamine.**

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CLUB DRUGS. The term *club drugs* is neither a pharmacological nor medical classification, but rather a cultural one referring to a chemically and psychoactively diverse group of drugs used and abused on the club and rave scenes of the late twentieth and early twenty-first centuries. Due to the ever-changing and novelty seeking nature of the youth-culture that spawned the term, no list of *club drugs* is likely to be complete, though most lists include MDMA, GHB, ketamine, rohypnol, methamphetamine, and LSD. One might add that changes in the youth culture may also render the club drugs obsolete as a useful grouping, as the cultural moment that brought them to the fore has largely passed. Further, use of the drug most commonly identified with the club drug class, MDMA, declined substantially in the late 1990s and early twenty-first century. Nonetheless, these drugs, together or apart, continue to be used and abused, particularly by young people with an experimental attitude towards drug use. A more useful name for the class might be *novelty drugs* owing to the fact that most users are attracted to these drugs by their actual or relative novelty compared to other drugs with more established reputations.

Whether the time of club drugs as cultural phenomena has passed or not, it is important that the cultural memory of their impact is not lost. Many young people faced with the choice to use drugs in 2008 were old enough to recall the cocaine epidemic of the 1980s, which in itself was in part a product of the loss of cultural memory of the cocaine epidemic of the 1930s. Like cocaine in its heyday, many club drug users took to these drugs because they seemed more benign than cocaine or heroin, the dangers of which were well known both to clinicians and the wider public. Lacking direct experience of the negative consequences of the use of these drugs led to a much more casual approach to their use than would have been the case with a hard drug such as heroin.

MDMA was not used recreationally until the 1980s, so information on the clinical consequences of its use and abuse was lacking both publicly and within the research community. Two decades later, due to research and clinical experience, the adverse consequences of MDMA use and abuse were more widely known. The lesson here is that experimenting with drugs is precisely that, an experiment, and often one whose result is more negative than anticipated.

MDMA is a psychoactive drug that emerged as a recreational drug in the mid-1980s, though it was first synthesized decades earlier. It is an amphetamine-derived hallucinogen, sometimes described as an empathogen or entactogen due to the enhanced feelings of emotional and physical closeness to others it generates in many users. Although it had a reputation as a benign so-called love drug, MDMA contributed to hundreds of deaths in its short time as an abused drug. It has been linked to seizures as well as kidney and cardiovascular failure. MDMA has produced long-term neurotoxicity in animals and a number of frequent human users have exhibited long lasting cognitive and emotional deficits.

Both rohypnol and GHB gained notoriety as *date-rape drugs* due to their criminally abused propensity for impairing memory and inducing unconsciousness. Again, both were fairly new to the world of recreational drug use, although rohypnol belongs to the same class of drugs, the benzodiazepines, as Valium, a drug with a well-known history of abuse. GHB, by contrast, is produced naturally in the human brain at low concentrations and may be involved in the regulation of sleep architecture. These drugs are especially dangerous when used with alcohol, which exacerbates their depressant effects often leading to stupor, respiratory depression, and in some cases coma and death. Like alcohol, GHB and rohypnol seem to cause an increase in violent behavior in some users. Another similarity to alcohol is the relative ease with which use of these drugs can result in overdose, dependency, and severe withdrawal syndromes. These drugs have been linked to such a disproportionate number of negative events that as of 2008 many countries had opted to increase restrictions on their use.

Methamphetamine has a long and well-documented history of abuse and toxic effects. Its appearance on the club scene seems to be linked to its low cost and the negative perception of cocaine as an alternative psychostimulant. Methamphetamine is substantially more toxic to the brain and liver than cocaine but it shares some of cocaine's potentially lethal effects on the cardiovascular system. Amphetamine use has also been linked to toxic psychosis.

Ketamine is a dissociative anesthetic formerly used in humans but subsequently largely restricted to veterinary use. Ketamine shares its major site of action with phencyclidine (PCP) and, like the latter drug, can produce many of the symptoms of psychosis in humans, including hallucinations and indifference to pain or death. Given that chronic PCP use has been associated with the development of long-term psychosis, it seems likely that this may prove to be a risk with ketamine as well. Ketamine is thought to have few other toxic effects, and some studies have demonstrated its potential as an acute antidepressant when used in low doses.

LSD is another drug with a well-known history of misuse and abuse. Its dangers lie in its hallucinogenic properties, which may cause users to physically harm themselves or others. LSD also seems to aggravate depression and psychosis. Outside its intense psychological effects LSD has few, if any, physiological side effects even when taken at doses well in excess of those used recreationally.

Club drugs are hardly risk-free, as has been made abundantly clear by many hospital admissions as well as basic and clinical research. A particularly risky and difficult-to-analyze aspect of the club drug phenomena is that most club drug users use several of these drugs as well as tobacco and alcohol. With such a variety of drugs being abused by individual users, toxic and other dangerous results are far more likely to occur and be less predictable in terms of long-term consequences.

See also **Amphetamine; Hallucinogens; Lysergic Acid Diethylamide (LSD) and Psychedelics; MDMA; Methamphetamine; Phencyclidine (PCP); Psychomotor Stimulant.**

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COCA PASTE. Coca paste is the first crude extraction product of coca leaves from the coca plant; it is obtained in the process of extracting cocaine from these leaves. The leaves are mashed with alkali and kerosene and then sulfuric acid (and sometimes also potassium permanganate). The result is an off-white or light-brown paste containing 40 to 70 percent cocaine, as well as other alkaloids, benzoic acid, kerosene residue, and sulfuric acid (ElSohly, Brenneisen, & Jones, 1991). Peruvian and Bolivian paste is illegally exported to Ecuador or Colombia, where it is purified into cocaine hydrochloride and then illicitly shipped to markets throughout the world. Although cocaine is the major component of coca paste, the paste is chemically complex, reflecting additives used by the clandestine laboratories performing the extraction from the coca leaves.

Coca paste, also called cocaine paste or pasta, is smoked, primarily in Latin American countries, by mixing about 0.2 ounces (0.5 g) of it with tobacco (called "tabacazo") or with marijuana (called "mixto") in a cigarette. When this dab of coca paste is smoked with tobacco, only 6 percent of the cocaine reaches the smoker—but because most of the paste samples contain significant amounts of manganese as well as several gasoline residues, the inhaled condensate is an extremely toxic substance. Despite the low bioavailability of cocaine from coca paste when it is smoked, use of this illegal substance by the smoking route reached epidemic proportions in Latin America in the late 1970s. More recently, coca paste smoking has been reported in the Netherlands, the Antilles, Panama, and the United States, although the level of use remains very low.

The effects of coca-paste smoking have been reported to be as toxic as those seen after intravenous or smoked cocaine (i.e., crack) in the United States. In fact, coca-paste smokers can achieve cocaine blood levels comparable to those seen in users injecting or smoking cocaine (Paly et al., 1980). Smoking the paste leads to an almost immediate euphoric response, and users smoke it repeatedly. As with smoking cocaine (freebasing), large quantities of the paste are taken repeatedly within a single smoking session, which is terminated only when the drug supply is depleted. Users report a dysphoric response (unease, illness) within about thirty minutes after smoking, so more paste is generally smoked at this time if available.

Substantial toxicity has been reported for chronic use of the coca-paste—tobacco combination, with users smoking it repeatedly, and progressing from stimulant-related effects and euphoria to hallucinations and paranoid psychoses. In fact, studies carried out in Peru defined a mental disorder of coca-paste smoking, made up of four distinct phases—euphoria, dysphoria, hallucinosis, and paranoid psychosis (Jeri et al., 1980). Since substantial amounts of paste are smoked at one time, the paranoid psychosis seen after chronic stimulant use has also been reported for paste use. As with cocaine abusers, experienced users of coca paste usually turn to criminal activities to support their illicit drug use.

See also **Bolivia; Crime and Drugs; Pharmacokinetics: General; Psychomotor Stimulant.**

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COCA PLANT. The coca plant is a cultivated shrub, generally found in the Andean Highlands and the northwestern areas of the Amazon in South America. The plant, however, can be grown

in many parts of the world and in the early part of the twentieth century much of the cocaine used in medicine was obtained from plants grown in Asia. Of the more than 200 species of the genus *Erythroxylon*, only *E. coca* variety *ipadu, E. novogranatense*, and *E. novogranatense* variety *truxillense* contain significant amounts of cocaine, ranging from 0.6 to 0.8 percent. In addition to cocaine, the leaves of the coca plant contain eleven other alkaloids, although no others are extracted for their euphorogenic effects.

Coca plants have long histories of use for both their medicinal and stimulant effects. Coca leaves are believed to have been used for well over a millenium, since archeological evidence from Peruvian burial sites of the 6th century CE suggests coca use. In fact, ancient Indian legends describe its origin and supernatural powers. The Inca called the coca plant a "gift of the Sun God," and attributed to it many magical functions. The Inca and the other civilizations of the Andes used coca leaves for social ceremonies, religious rites, and medicinal purposes. Because of their energizing property, coca leaves were also used by soldiers during military campaigns or by messengers who traveled long distances in the mountains. Under the Spanish conquest of the sixteenth century, coca plants were systematically cultivated and the custom of chewing coca leaves or drinking coca tea was widely adopted as part of the Indian's daily life in South America. Use of coca leaves as both a medicinal and a psychoactive substance continues to be an integral part of the daily life of the Indians living in the Andean highlands. Substantial societal controls have existed concerning the use of these leaves, and minimal problematic behavior related to use of the coca leaves has been reported.

In the highland areas of Peru and Bolivia, and less frequently, in Ecuador and Colombia, the dried leaves are mixed with lime or ash (called "tocra") and both chewed and sucked. A wad containing 0.4 to 1 ounce (10 to 30 g) of leaf is formed, and daily consumption by coca-leaf chewers is between 1 and 2 ounces (30 and 60 g). The Indian populations in the Amazonian areas, however, crush the dried leaves, mix the powder with an alkaline substance, and chew it. Coca leaves are chewed today in much the same way that they were chewed hundreds of years ago.

Substantial cocaine plasma levels can be attained when coca leaves are chewed along with an alkaline substance, which increases the bioavailability of the drug by changing its pH. Volunteers allowed to chew either the leaf or the powdered form of coca mixed with an alkaline substance reported numbing in the mouth and a generally stimulating effect which lasted an average of approximately an hour after the coca chewing was begun (Holmstedt et al., 1979). This time-course corresponded to the ascending limb of the cocaine plasma-level curve, suggesting that the effect was cocaine-induced. Absorption of cocaine occurs from the buccal mucosa (inner cheek wall) as well as from the gastrointestinal tract after saliva-containing coca juice is swallowed. In fact, plasma concentrations in coca chewers are about what would be predicted if a dose of cocaine equivalent to that in the leaves was administered in a capsule (Paly et al., 1980).

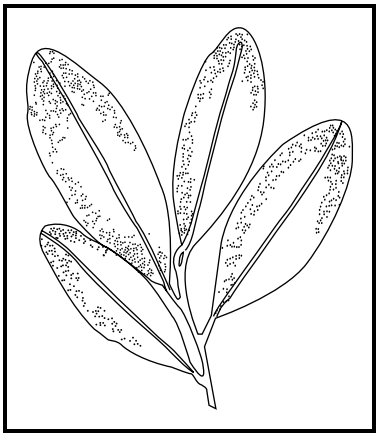

Figure 1. Coca leaf. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Bolivia; Coca Paste; Colombia.**

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COCA/COCAINE, INTERNATIONAL.

When Amerigo Vespucci landed on the coast of what is now Venezuela in 1499, the first thing he saw was a group of native peoples chewing coca leaf. The captain and most of his crew thought the practice disgusting, but it did not take Spanish colonists long to discover that chewing small amounts of coca leaf gave them more energy. In 1559, the Spanish herbalist and physician Nicholas Monardes, who practiced in the port city of Seville, heard stories about coca and saw the plants collected by those returning from the New World, making him one of the first Europeans to learn about coca. He wrote, "Surely it is a thyung of greate consideration, to see how the Indians are so desirous to be deprived of their wittes, and be without understanding" (Monardes, 1925). The fact that no one became seriously ill from chewing too many of the leaves suggested that other components of the leaves caused nausea, and indeed those who chewed the plant developed unpleasant side effects long before they had ingested enough to become ill. It is now known that plasma levels never reach very great heights in leaf chewers, or in coca tea drinkers, which explains why few other cocaine-induced effects occurred among the Indians—and why reports of cocaine-related deaths among Indian coca chewers and tea drinkers have remained rare until the present day.

EARLY CULTIVATION OF COCA

Spanish settlers started arriving in Peru even before Francisco Pizarro's army completely subjugated the Incas in the 1530s. Immigrants were given tracts of land and an allotment of slave laborers. Initially, the occupiers paid relatively little attention to coca, but when they realized how much coca leaf the Indians were chewing, and how badly they wanted cocaine, it didn't take long for coca to become a cash crop. In fact, coca growing became so profitable that the immigrant farmers stopped growing their normal staple crops and devoted all of their acreage to coca cultivation. The situation reached crisis proportions when the colonial government was unable to procure enough hay to feed the horses it had also imported (Gagliano, 1994).

Food shortages became severe, and the second Spanish viceroy was forced to pass legislation requiring crop substitution and prohibiting farmers from devoting more than 10 percent of their land to coca growing. The prohibition was largely ignored, however. In 1545, silver was discovered high in the mountains, at Potosi. The Indian slaves refused to work in the abysmal conditions of the mines without their ration of coca. King Phillip badly needed the cash that the silver would bring, and so coca was supplied to the workers. Attempts at crop substitution were abandoned at this time, and the government decided instead to tax coca production. There was so much money to be made selling coca, however, that the taxes proved little disincentive to the growers. This arrangement came to an end when the Spanish lost control of the New World, which more or less freed the indigenous peoples from slavery.

Cocaine abuse did not become an issue for Europeans until the late 1800s. For one thing, supplies of coca leaf were scarce. For another, coca travels poorly, and it took up a great amount of room in ships' holds. So, after they had shipped home all the plundered gold and silver, the Spanish made sugar, rather than coca, their export of choice. The exportation of coca leaf to Europe simply made no economic sense, at least not when there were more profitable alternatives, and sugar was in great demand in Europe. Markets evolve, however, and the near simultaneous occurrence of three important technical advances turned the export market on its head and made the exportation of coca into an attractive proposition.

COCA COMES TO EUROPE

All during the time that the Spanish occupied the New World, they took great pains not to let the rest of Europe know what was going on in the New World, and all knowledge of the place was strictly embargoed. When the Spanish embargo ended, coca growers found better ways to preserve coca leaves during transit, and the French discovered a way to make a wine from the coca leaves. The wine proved to be an immensely popular product, and it was soon for sale worldwide. In spite of the wine's popularity, there was never a case of toxicity reported from its use. This was because the natural properties of the coca leaf prevented it from being abused. The process for isolating pure cocaine from coca was not discovered until 1860, but French pharmacists discovered a way to partly extract

cocaine from coca, leaving most of the waxes and tannins behind. They added coca leaves to average Bordeaux wines (the Dutch preferred Malaga wine)—in a ratio of roughly ten parts wine to one part dried, ground, coca leaves—let the mixture steep for a few days, and then removed the leaves, thereby creating "coca wine."

An average glass of this wine contained only 6 milligrams of cocaine, but this was enough, when combined with the wine, to provide a pleasurable experience. Attempts at raising the cocaine concentration by adding more leaves were doomed to failure, because when too many leaves were added, or if the leaves were allowed to steep too long, the final product contained tannins and wax in far greater concentrations than were contained in the handful of leaves chewed by the Indians, which would have made it undrinkable. Still, even with its low cocaine content, coca wines became extremely popular as relatively harmless stimulant tonics.

THE EUROPEAN COCA INDUSTRY

As the New World opened up to explorers, contract botanists working for the Royal Botanical Gardens at Kew, outside of London, began to send coca seeds back to England. Although many more exist in the wild, there are only four cultivated variations of *Erythroxylum taxa*: *E. coca* var. *coca*, *E. novogranatense* var. *novogranatense, E. coca* var. *ipadu*, and *E. novogranatense* var. *truxillense* (Johnson et al., 2005). Some of the species contain a good deal more cocaine than others, however. Seeds from the most popular commercial variety of coca arrived at the Kew Botanical Gardens in 1869. They were collected from the area south of Cuzco, in Peru. Plants from these seeds were continuously cultivated at Kew for 40 years, and they were also sent to other botanical gardens administered by Kew. At one time there were British-owned coca plantations operating in Africa, India (where Darjeeling tea is now grown), and Malaysia. Fortunately for the Dutch planters in Java, their government was not enthused about the prospects of growing coca, for they already had a substantial problem with opium cultivation and addiction. As a consequence of this delay, the Dutch botanical gardens, located outside of Jakarta, entered the cocaine market only after the Kew plants had become widely disseminated to British dependencies. However, the coca plants obtained by the Dutch growers contained more than twice as much cocaine as the commercial varieties grown in South America, which no doubt explains why, in the early 1900s, sales from Java eclipsed those from South America (Reens, 2003). Unfortunately, not much is known about the origin of the root stock used by the Dutch. The original seedlings were purchased from a Brussels trading company, Herman Linden and Sons, but how that company obtained the plants, or where they obtained the plants, is not known.

MEDICAL USES OF COCAINE

In 1860 Albert Von Niemann (1834–1861), a doctoral student at the University of Göttingen, devised a method for extracting cocaine hydrochloride from coca leaves, and experimentation with medical uses for the new substance soon began. During the 1870s, the work of Dr. Alexander Hughes Bennett in Edinburgh stimulated further investigation. (In their book *Opium and the People* [1987] Virginia Berridge and Griffith Edwards discuss the competition among British doctors to report on the sustaining properties of the coca leaf during exertion.)

Shortly after Von Neiman's discovery, the German company Merck of Darmstadt began producing minute quantities of cocaine (less than a few ounces a year). Because it was so expensive, there was no commercial market for purified cocaine at the time, and no one in the medical community yet had a clear idea of the benefits of cocaine. Nonetheless, Merck continued to produce small amounts of the drug every year, if for no other reason than to prove they were the world's greatest pharmaceutical chemists. In 1884, however, the company was rewarded for its perseverance. In that year Sigmund Freud (1856–1939) published his famous paper "Über Coca," in which he recommended the use of cocaine for the treatment of a variety of unrelated medical conditions—including the treatment of morphine addiction.

Much more important than Freud's discovery was the one made by Carl Koller (1857–1944), Freud's roommate in the dormitory at Vienna General Hospital. Freud and Koller had experimented with cocaine by taking it themselves and observing the effects they experienced. On a weekend visit with his fiancée Martha Bernays (1861–1951),

Freud demonstrated the drug's marvelous effects to her. At the same time, Koller was busy discovering that cocaine was a local anesthetic. Acting on a hunch, he put some drops of cocaine into a guinea pig's eye and discovered that the eye became insensitive to pain. Koller then tried it on himself and confirmed that his discovery was valid (Oeppen, 2003).

Before he made his great discovery, Koller was living in poverty and had to convince a friend (an eye surgeon) to go to the upcoming meeting of the Heidelberg Ophthalmologic Society and present a paper describing his findings. The paper was read on September 19,1884. An American named Henry Noyes was in the audience, and he mailed an account of the meeting back to the editors of the *New York Medical Record*. Noyes's account was published on October 11, 1884, less than one month after the discovery was announced (Noyes, 1884). The discovery of cocaine's local anesthetic properties led to an explosive increase in the demand for the drug, as well as a huge increase in its price. In 1883, Merck had produced only a few ounces of cocaine in the entire year, but the following year the company's production was measured in tons.

The demand for cocaine was more than adequately met by the venture capitalists and pharmaceutical houses of the day. Coca plantations sprang up all over the world, and there was soon a predictable glut of cocaine. As a result, prices began to drop and competition for customers began to increase. The Parke-Davis Company and Merck found themselves in a battle for world dominance of the cocaine market. The Parke-Davis product was thought to be of better quality at a lower price, and the company built on that reputation by providing Freud with samples and an honorarium.

ADDICTS, DOCTORS, AND QUACKS

The first American to experiment with cocaine anesthesia was Dr. William Stewart Halsted (1852–1922), a visiting surgeon at Bellevue Hospital in New York City. Within a week after reading of Koller's discovery, Halsted and his associates Richard Hall and Frank Hartley had experimented on themselves, on their surgical colleagues, and on an occasional patient. Halsted built upon Koller's initial work, and he observed that when cocaine was injected into nerves, it blocked the perception of pain within the area supplied by those nerves. Halsted and his group published their first paper on cocaine-induced nerve blocks just six weeks after Koller's announcement. Unfortunately, Koller also became addicted to cocaine, and he remained addicted to the drug even after he was appointed professor of surgery at Johns Hopkins Medical School. His friend, the famous physician William Osler, was a professor of medicine at the same school, and he eventually cured Halsted of his addiction—but only by addicting him to morphine instead. Halsted remained addicted to morphine until his death in 1922 (Colp, 1984).

Surplus cocaine at cheap prices meant that winemakers no longer had to bother soaking coca leaves in wine. Instead, they just added a pound or so of cocaine to a vat of cheap red wine. The final product contained anywhere from 60 to 120 milligrams of cocaine per glass, a considerable increase over the benign 6 milligrams in the old French versions. The practice of spiking inferior product with purified cocaine was not just limited to winemakers, however. The producers of patent medicines, the "snake oil" remedies so popular in the early twentieth century, began adding enormous amounts of cocaine to their wares. Predictably, reports of death and injury soon became a regular feature of medical journals all around the world (Adams, 1905).

In the early 1900s there were literally thousands of these remedies for sale. Their chief ingredient was alcohol, but cocaine and opium were almost always part of the formula. Dr. Fahrney's Teething Syrup, which contained heroin, surely must have been a very effective agent with which to console teething children, while Casebeer's Coca Calisaya was advertised as an "agreeable and efficient tonic," capable of "sustaining the strength under extreme physical exertion," not to mention curing those "enfeebled by sickness or disability." This product was composed mainly of alcohol and cocaine, with some cherry flavoring added. Perhaps the most outrageous of the products was Coca-Bola chewing gum. The makers of the gum recommended it be used "at occasional intervals throughout the day," even though each stick of gum contained 710 milligrams of cocaine (Adams, 1905). In order to put this amount in perspective, a modern "line" of cocaine weighs in at 50–70

milligrams, and a piece of rock cocaine, or "crack," contains even less. Chewing one stick of the gum would have amounted to "snorting" 10 lines of cocaine at one time. The predictable result was toxicity and addiction.

The end of World War I brought an end to the legitimate German cocaine industry, which comprised a cartel of drug makers who produced cocaine in addition to their other products. Article 295 of the Versailles Peace Treaty incorporated within it all of the previous provisions of the Hague Convention of 1912, which Germany had refused to sign. Manufacturers were prohibited from selling cocaine except for explicitly medical purposes. The clandestine laboratory had yet to be invented, and the antidrug legislation was thus intended to rein in legitimate drug makers. Nonetheless, low-level cocaine consumption continued among the wealthy of Berlin and Paris.

COCAINE GOES UNDERGROUND

By the 1920s nearly everyone in the civilized world knew someone whose life had been adversely affected by cocaine, and very few were particularly anxious to repeat the experience. This is clearly reflected in the literature of the time. The most famous writer to cash in on the problem of the cocaine craze was Arthur Conan Doyle (1859–1930). Doyle had trained as an ophthalmologist at the Vienna General Hospital, which was home to Freud and Koller, so it is hardly surprising that his fictional character Sherlock Holmes knew all about the properties of cocaine (Musto, 1989).

In 1919 Sax Rohmer (born Arthur Henry Ward, 1883–1959), the creator of the Fu Manchu stories, wrote a novel titled *Dope: A Story of Chinatown and the Drug Traffic*. The book was a thinly veiled retelling of the events surrounding the cocaine-related death of an East End actress named Billie Carleton (nee Florence Stewart, 1896–1918). In 1926 another British novelist, Aleister Crowley (1875–1947) wrote *Diary of a Drug Fiend*, in which the hero, Peter Pendragon, is introduced to cocaine and heroin by his girlfriend. The story was set in London's Mayfair district and it, too, seemed to be based on the Billie Carleton story.

In less than 50 years from the time it was first purified in 1860, cocaine had gone from a wonder drug to a scourge. Cocaine users were looked upon as deviant losers, although cocaine abuse continued in Europe at a low level until the beginning of World War II. Most of the cocaine sold in Europe came from sources in Southeast Asia and traveled via supply lines that remained intact for much longer than those that served the United States. At the time, cultivation in South America was in decline, which affected the U.S. market, but production in Southeast Asia persisted unabated until the war in the Pacific finally disrupted that supply.

One of the lesser-known chapters of history involves Japan's adventures in the cocaine trade. Japan bought much of Indonesia's coca output and maintained its own coca plantations in Taiwan (then the Japanese possession called Formosa) and Iwo Jima. Coca leaves were shipped to Tokyo for refining, and the cocaine was sold on the black market, both by drug smugglers and by the Japanese government itself. The government had a competitive advantage because it owned a major interest in Japan's major shipping line. In fact, Japan partly financed the occupation of China by selling cocaine and heroin to the Chinese (Karch, 1998). At the Tokyo War Crimes Trials that followed World War II, Japan was charged with crimes against humanity not only for the Nanking Massacre, but also for drug dealing. One of the exhibits used at the trials was a copy of a Japanese war bond, for which payment was guaranteed by sales of narcotics in occupied China.

COCAINE'S RESURGENCE

Cocaine reemerged as a major drug of abuse and an illegal commodity on world markets in the mid-1970s. This could never have occurred were it not for a waning of both individual and social memories of the negative effects of cocaine. Readers of the popular press in the early 1980s would never have guessed that cocaine was toxic, or that there had ever been any previous problems with the drug. At the time, cocaine had almost disappeared from world markets, and prices were so high that only the very rich, and particularly entertainment and fashion celebrities, could afford the drug. In his autobiography, the great jazz musician Miles Davis (1926–1991) wrote that in 1972 he was earning more than half a million dollars a year, and that he was spending most of this money on cocaine.

In November 1983, the British medical journal the *Lancet* editorialized about cocaine, writing that it "may thus be reasonably safe when used in a socially well-integrated fashion by people living in a stable community," and at the same time insisting that "its dangers must be overrated." This view confirmed the opinions espoused by many experts in the United States. That the *Lancet* could make such a statement in 1983 indicates that: (1) the authors of the editorial had had little exposure to chronic cocaine users, (2) they knew even less about the history of the drug, and (3) not much cocaine was available in the country at that time.

In 1989, the Reuters News Service reported, with some concern, that cocaine seizures in the United Kingdom had reached 227 kilograms in that year, amounting to an increase of 27 percent from the previous year (*Philadelphia Inquirer*, January 19, 1989). As late as May 2008, the British press still considered the seizure of a mere 140 kilograms of cocaine as worthy of mention. By way of comparison, at roughly the same time, the U.S. Coast Guard reported it had interdicted 21 tons of cocaine sitting in plain sight on the deck of a tramp steamer (*Washington Post*, March 21, 2007).

Even though the extraction process used today is not very different from the process used in the 1870s, the coca plants grown in the early twenty-first century are somewhat different from those of the nineteenth century. For one thing, they contain more cocaine, though whether this is a result of old-fashioned cross breeding or genetic engineering is hard to say. DNA analysis done in the early twenty-first century showed that modern coca leaves contain far more cocaine than those from the first decade of the twenty-first century (Johnson, 2003).

In addition, the production and sale of cocaine increased dramatically in the 1970s. In the mid-1970s, sales of cocaine by the Medellin cartel of Colombia amounted to, at most, 40 kilograms of cocaine a week. By the end of the 1970s, however, that amount had grown to several hundred kilograms, and by the early 1980s the cartel's output was measured in tons per week. By the start of the 1990s, Boeing 727s containing 5 to 7 tons of cocaine made weekly trips across Mexico to the United States. Further, as had been the case 100 years earlier, cocaine prices began to fall. In Medellin in 1982, one kilogram of pure cocaine sold for $20,000, but by early 1984 the wholesale delivery price had dropped to only $4,000 per kilogram. This occurred partly because Bolivia had also gone into the cocaine refining business, and partly because production had expanded in all of Colombia's neighboring countries as well (Office of National Drug Control Policy, 1996).

CRACK COCAINE

The technical advance that really drove the new wave of cocaine abuse was the advent of crack. This was, in fact, exactly the same drug that had been responsible for so much misery a century earlier, but it was now in a different, more dangerous, form. The first crack smokers began to appear at psychiatric clinics in 1986 in the Bahamas, which in the mid-1980s was an important part of the transshipment route for cocaine from South America. Smoking crack enables more cocaine to get into the body more quickly, thereby achieving higher blood concentrations—and thus higher "highs." In the process, all the natural safeguards provided by using coca leaf, either by chewing or by drinking coca-wine, were bypassed. Crack was an irresistible force, and with so much cocaine available, the only difference between 1884 and 1984 was the magnitude of the problem.

When crack made its debut in Europe, it was considered just one of many drugs being abused, and it was therefore accorded no special status. Yet the press, both in the United Kingdom and the United States, had unfairly conflated the "desperate state of America's inner cities, whose problems crack had worsened but not created" with the effects of the drug itself (Royal College of Psychiatrists, 2000). A study of South London drug addicts published in the *British Journal of Addiction* in 1990 found that only 1 percent of the study subjects smoked cocaine in the absence of other drugs, while the majority of other attendees combined their crack with methadone or heroin (Strang, Griffiths, & Gossop, 1990). The study also found that the number of crack smokers had increased from 13 percent to 29 percent in just over a decade.

COCAINE IN THE TWENTY-FIRST CENTURY

Traditionally, coca is grown high in the Andes. In 2008, however, drug and plant seizures suggested

that coca cultivators had managed to hybridize (or perhaps even genetically engineer) a new strain of coca that grows very well in the Amazon jungle (Carroll, 2008). In spite of intense efforts and great expenditures on the part of the United States, coca supplies do not appear to have decreased significantly during the first years of the twenty-first century. According to the United Nations, in 2005, slight production decreases in Bolivia and Peru were more than offset by increases in Colombia. In 2006, meanwhile, just the reverse occurred, with decreased Colombia production offset by increases elsewhere in the Andes (United Nations Office on Drugs and Crime, 2008).

The most recent data suggest that, if anything, the situation has deteriorated further. On June 18, 2008, the United Nations Office on Drug and Crime (UNDOC) released its yearly Andean coca production survey, showing a marked increase in coca cultivation. According to the most recent data, the total area of land under coca cultivation in Bolivia, Columbia, and Peru in 2007 was thought to be 181,600 hectares, amounting to a 16 percent increase over 2006 and the highest level since 2001. The increase was driven by a 27 percent rise in Columbia (for a total of 99,000 hectares), and smaller increases of 5 and 4 percent, respectively, in Bolivia and Peru.

Surprisingly, even though coca cultivation has increased, the actual amount of cocaine produced was unchanged. In 2007, global potential production of cocaine was estimated at 994 metric tons, essentially the same as the 984 tons reported in the 2006 survey. The UNODC coca survey shows that almost half of Columbia's cocaine production, 288 tons, and one-third of the cultivation (35,000 hectares) came from just 10 of Columbia's 195 municipalities (5%).

The head of UNODC Costa was quoted as saying "Just like in Afghanistan, where most opium is grown in provinces with a heavy Taliban presence, in Columbia most coca is grown in areas controlled by insurgents." Even so, Columbian cocaine production remained almost unchanged in 2007 at 600 tons.

Citizens of the United States continue to be the world's main cocaine consumers, but the amount consumed elsewhere in the world is rising steadily. In the early twenty-first century, 90 percent of the cocaine smuggled into the United States originated in Colombia and passed through the Mexico-Central America corridor. Drug trafficking in all of North America during this period has been controlled by powerful, well-funded criminal organizations. These organizations have waged war against the Mexican authorities in an attempt to keep Mexico the main transit route for cocaine shipments to the United States. Criminal organizations in Mexico have also continued to profit from the sale of heroin, methamphetamine, and cannabis in the United States (International Narcotics Control Board, 2008).

Europe is the second largest market for cocaine, and seizures have risen significantly in Finland, Germany, Ireland, Portugal, Spain, and Switzerland. Outside of the United States, the highest rates of cocaine abuse are in Spain, the United Kingdom, and Italy. In 2004 in the United Kingdom, 5.2 percent of 16- to 19-year-olds and 14.1 percent of 20- to 24-year-olds reported having cocaine in the previous year (Reuter & Stevens, 2007). Interpol estimates that 200 to 300 tons of cocaine make their way into Europe every year. Just five years ago most British cocaine seizures were measured in kilograms. Now they are measured in tons (Bureau for International Narcotics and Law Enforcement Affairs, 1999).

John Walters, the head of the White House Office of Narcotics and Drug Control Program, said at a 2007 press conference in Haiti that cocaine production had risen to 1,400 metric tons in that year (Schneider, 2008). If correct, this figure represents a 40 percent increase over yearly production for each of the previous five years of "Plan Colombia," a multibillion dollar aid package designed to eradicate coca production in South America. (According to the International Narcotics Control Board [2008] South American production stood at 1,008 metric tons in 2004, 980 metric tons in 2005, and 984 metric tons in 2006.) The supply side of the cocaine market has proven to be adaptable and resistant to eradication efforts, in spite of the vast tracts of land that have been deforested. Instead, the use of fertilizers and pesticides, as well as better production technologies, has improved coca yields.

U.S. demand is easily met by a fraction of the amount that is actually produced in South America,

and the remainder is now being diverted to the United Kingdom and Europe, via the coast of Portugal and Africa. In its 2008 annual report, the International Narcotics Control Board drew attention to the fact that West Africa is rapidly developing into a major smuggling route for cocaine from Latin America on its way to Europe. (The African country of Guinea Bissau may now be the world's first true narco-state, where all government officials are the employ of various Colombian cartels, and the only reliable source of income is drug trafficking.) One troubling side effect of this phenomenon is that in the countries of western Africa, cocaine use has also increased by the people who live there—and who now derive much of their income from cocaine sales. Rising levels of seizures in Africa, especially along the Gulf of Guinea and off the coast of Cape Verde, show that Africa's role as a transshipment point is rapidly increasing.

Efforts at interdiction appear to have been more successful than eradication. The United Nations believes that as much as 42 percent of all the cocaine produced in 2006 was interdicted, largely as a result of improved cooperation among law enforcement bodies around the world. Nearly 60 percent of all global cocaine seizures in 2005 took place in South America, the Caribbean, and Central America, while North America accounted for 28 percent, and Europe for about 14 percent.

The only remaining legitimate use of cocaine is for head and neck surgery. Unlike any other local anesthetic, cocaine causes blood vessels to contract. By injecting an area with cocaine, the surgeon not only eliminates the pain of surgery, but also greatly reduces blood loss, a goal in all surgical procedures. At the end of World War II, a League of Nations committee estimated that total, worldwide medical consumption amounted to less than 10 tons per year (Atzenwiler, 1944). In 2007, estimated production approached 1,000 tons per year (National Drug Intelligence Center, 2007). However, the amount needed for legitimate medicinal cocaine use remains at only 10 tons.

See also **Cocaine; Freud and Cocaine; International Drug Supply Systems.**

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STEVEN B. KARCH

COCAETHYLENE: IMMUNOLOGIC, HEPATIC, AND CARDIAC EFFECTS.

Cocaethylene, a compound synthesized by the body when cocaine is used concurrently with alcohol, was first identified in 1979. Because the half-life (the time required for the body to break down and eliminate half of the substance) of cocaethylene is three to five times that of cocaine, it extends the euphoric sensation of cocaine and lessens the dysphoria (unpleasantness or discomfort) associated with its cessation. In 2006, according to the National Survey on Drug Use and Health, 33

percent of the nation's 17 million heavy drinkers also abused illicit drugs, including cocaine. Use patterns for the combination of alcohol and cocaine appear to differ according to the form of cocaine that is abused (Gossop et al., 2006). Users of powder cocaine appear to increase both alcohol and cocaine consumption when the two agents are used concurrently whereas users of crack cocaine decrease their consumption of alcohol during high-dose episodes. Crack cocaine users are also likely to reserve alcohol for use at the end of crack-using sessions (Gossop et al., 2006).

Cocaethylene, also known as ethylcocaine, ethylbenzoylecgonine, and benzoylecgonine ethyl ester, is reported to be more damaging to both the heart and brain than cocaine. Although the mechanism by which the combination of cocaine and ethanol may be particularly harmful to the cardiovascular system is unknown, two hypotheses have been proposed to explain this phenomenon:

1. It may significantly increase the myocardial oxygen demand and simultaneously diminish supply, leading to a marked supply and demand imbalance. In human volunteers, the use of both drugs produces a greater increase in heart rate than either substance alone;
2. The concomitant ingestion of cocaine and ethanol can lead to the production of a metabolite (breakdown product) that induces marked constriction of the coronary arteries, leading to myocardial ischemia (impaired function due to inadequate oxygen), infarction (cell death), and/or sudden death of the individual.

Laboratory models for the formation of cocaethylene have been difficult to develop. In one study, dogs failed to produce cocaethylene following the administration of cocaine intravenously. However, when the ability of human and dog liver cells to produce cocaethylene was compared, cocaethylene formation was greater in the dog. The investigators concluded that the route of cocaine administration might be an important factor in the formation of cocaethylene. In a study of primates, the effects of intravenously administered cocaine on extracellular dopamine, cocaethylene, and cocaine were equal in their ability to increase extracellular dopamine in the caudate nucleus. Similar to cocaine, cocaethylene inhibits the dopamine transporter, thereby blocking the reuptake of dopamine from the synapse. Further studies appear warranted in species that more closely resemble humans to determine the pathways and significance of the cocaine and ethanol combination.

Animal studies suggest that the toxicity that results from combined cocaine and ethanol use is not due to enhanced sensitivity to alcohol in cocaine abusers. In rats, cocaethylene exposure during the fetal brain growth spurt period slows brain growth. Cocaethylene is also a neuroteratogen (adversely affecting the development of the nervous system) as indicated by altered concentrations of catecholamine (such as norepinephrine) and indoleamine (such as serotonin) neurotransmitters in developing brains, with a region-specific alteration in neurotransmitter levels following six days of cocaethylene exposure. It also appears that cocaethylene is more similar to ethanol than cocaine in terms of adverse effects on neural development.

Cocaethylene is now recognized as playing a significantly damaging role in brain development and function and as a cardiovascular risk factor. Because cocaine and alcohol are frequently used concurrently, the negative effects of cocaethylene have substantial public health implications. However, much remains to be learned regarding the reinforcing (rewarding) effects of cocaethylene and its mechanism of adverse effects.

See also **Alcohol; Benzoylecognine; Cocaine; Complications: Cardiovascular System (Alcohol and Cocaine); Complications: Immunologic; Complications: Liver (Clinical); Drug Interactions and Alcohol; Fetus, Effects of Drugs on the; Reward Pathways and Drugs.**

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COCAINE. The abuse of cocaine has become a major public-health problem in the United States since the 1970s. During that period it emerged from relative obscurity, when it was described by experts as a harmless recreational drug with minimal toxicity. By the mid-1980s cocaine use had increased substantially, and led to drug taking at levels that caused severe medical and psychological problems. Cocaine (also known as *coke*, *snow*, *lady*, *crack*, and *ready rock*), is an alkaloid with both local anesthetic and psychomotor stimulant properties. Users generally take it in binge cycles, using it repeatedly within hours or days, alternating with periods of non-use. Many users are recalcitrant to treatment, and the substantial criminal penalties for possession and sale have not yet reduced its heavy use. In fact, information in 2007 from the Community Epidemiologic Work Group (CEWG, 2007) showed an increase in cocaine/crack use in several regions of the United States.

HISTORY

Cocaine is extracted from the coca plant (*Erythroxylon coca*), a shrub now found mainly in the Andean highlands and the northwestern parts of the Amazon in South America. The history of coca plant use by the cultures and civilizations that lived in these areas (including the Inca) goes back more than a thousand years, with archeological evidence of coca use found in their burial sites. The Inca called the plant a "gift of the Sun god" and believed that the leaf had supernatural powers. They used the leaves much as the highland Indians of South America do today. A wad of leaves, along with some ash, is placed in the mouth and both chewed and sucked. The ash helps extract cocaine from the coca leaf, and the cocaine is efficiently absorbed through the mucous membranes of the mouth.

During the height of the Inca Empire (eleventh through fifteenth centuries) coca leaves were reserved for the nobility and for religious ceremonies, since it was believed that coca was of divine origin. With the conquest of the Inca Empire by the Spanish in the 1500s, coca use was banned. The Conquistadors soon discovered, however, that coca was an aid to working in the high mountain air and served as an incentive for the Indians, so in 1569 King Philip II (1527–1598) declared that coca was not devilish and could be used.

Although glowing reports of the stimulant effects of coca reached Europe, coca use did not achieve popularity. This may have been because coca plants could not be grown in Europe, and the active ingredient in coca leaves did not survive the long ocean voyage from South America. After the German chemist Albert Niemann (1880–1921) isolated cocaine from coca leaves in 1860 and the drug was subsequently purified, it became more popular. Commercial endeavors aided its popularity by combining cocaine with wine (e.g., Vin de Coca), products that were enthusiastically and uncritically endorsed by notables of the time.

Both interest in and use of cocaine spread to the United States, where extracts of coca leaves were added to many patent medicines. Physicians began prescribing it for a variety of ills including dyspepsia, gastrointestinal disorders, headache, neuralgia, toothache, and more, and its use increased dramatically. By the beginning of the twentieth century, the harmful effects of cocaine were noted, and its utility was reassessed. As part of a broader regulatory effort, the U.S. government controlled its manufacture and sale. In 1914 the Harrison Narcotics Act forbade use of cocaine in over-the-counter medications and required the registration of those involved in the importation, manufacture, and sale of either coca or opium products. This substantially reduced cocaine use in the United States, and use remained relatively low until the late 1960s, when it moved into the spotlight once again.

MEDICAL UTILITY

Cocaine is a drug with both anesthetic and stimulant properties. Its local anesthetic and vasoconstriction effects remain its major medical use. Carl Koller (1857–1944) established its local anesthetic effect in the mid-1880s in experiments on the eye, but because it causes sloughing of the cornea, it is no longer used in eye surgery. Because it is the only local anesthetic capable of causing intense vasoconstriction, cocaine is beneficial in surgeries where shrinking of the mucous membranes and the associated increased visualization and decreased bleeding are necessary. Therefore, it remains useful for topical administration in the upper respiratory tract. When used in clinically appropriate doses and with medical safeguards in place, cocaine appears to be a useful and safe local anesthetic.

PHARMACOKINETICS

Cocaine can be taken by a number of routes of administration—oral, intranasal, intravenous, and smoking. Although the effects of cocaine are similar no matter what the route, some routes clearly contribute to the likelihood that the drug will be abused. The likelihood that cocaine will be taken for nonmedical purposes is related to the rate of increase in cocaine brain level (as measured by blood levels); routes that provide the largest and most rapid changes in brain level are associated with greater self-administration. The oral route, not used by cocaine abusers, is characterized by relatively slow absorption, and peak levels do not appear until approximately an hour after ingestion. Cocaine, however, is quickly absorbed when it is inhaled into the nose as a powder (cocaine hydrochloride). Because of its local anesthetic properties, cocaine numbs or "freezes" the mucous membranes; drug purchasers on the street use this to test for purity. When cocaine is used intranasally (*snorting*), cocaine blood levels, as well as subjective and physiological effects, peak at about 20 to 30 minutes, but reports of a "rush" are not as strong as when the drug is smoked or administered intravenously. Intranasal users report that they are ready to take a second dose of the drug within 30 to 40 minutes after the first dose. Although this was the most common way to use cocaine in the mid-1980s, it declined in popularity relative to smoked cocaine after the advent of crack mid-decade. Snorting cocaine powder appears to have risen slightly in the last 10 years, while smoking and injecting have decreased (DASIS, 2007).

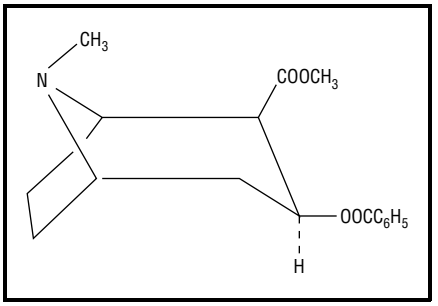

Figure 1. Chemical structure of cocaine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

When taken intravenously, venous blood levels peak virtually immediately, and subjects report a substantial rush. This route was, until the mid-1980s, traditionally the choice of the experienced user, since it provided a rapid increase in brain levels of cocaine with a parallel increase in subjective effects. The amount of cocaine in blood and brain drop in parallel with the stimulating effects of cocaine, and cocaine users report that they are ready for another intravenous dose within about 30 to 40 minutes. Users of intravenous cocaine are also more likely to combine their cocaine with heroin (i.e., a *speedball*) than are users by other routes.

In the mid-1980s smoking cocaine began to achieve popularity. Freebase, or *crack*, is cocaine base that is not destroyed at temperatures required to volatilize it. As with intravenous cocaine, blood levels peak almost immediately, and a substantial rush ensues after smoking it. Users can prepare their own freebase from the powdered form they purchase on the street, or they can purchase it in the form of crack, or *ready rock*. The development of a smokable form of cocaine provided a more socially acceptable route of drug administration (both nicotine and marijuana cigarettes provided the model for smoking cocaine), resulting in a drug that was both easy to use and highly toxic, since this route allowed for frequent repeated dosing with a readily available and relatively inexpensive drug. The use of intravenous cocaine, in contrast, was limited to those able to acquire the paraphernalia and willing to put a needle in a vein. The toxicity of the smoked route of administration is related, in part, to the fact that a potent dose of cocaine is available to anyone who can afford it.

Cocaine is frequently taken with other drugs such as alcohol, marijuana, or opiates. In 2006 in

the United States, many cocaine deaths involved more than one drug. When taken with alcohol, a metabolite (cocaethylene) forms that appears to be only slightly less potent than cocaine in its behavioral effects. It is possible that some of the toxicity reported after relatively low doses of cocaine might well be due to the combination of cocaine and alcohol.

Cocaine is broken down rapidly by enzymes (esterases) in the blood and liver. The major metabolites of this action (all relatively inactive) are benzoylecgonine, ecgonine, and ecgonine methyl ester, all of which are excreted in the urine. People with deficient plasma cholinesterase activity—fetuses, infants, pregnant women, patients with liver disease, and the elderly—are all likely to be sensitive to cocaine and therefore at higher risk for adverse effects than are others.

PHARMACOLOGY

Research has focused on the neurochemical and neuroanatomical substrates that mediate cocaine's reinforcing effects. Although a number of neurotransmitter systems are involved, there is growing evidence that cocaine's effects on dopaminergic neurons in the mesolimbic and/or mesocortical neuronal systems of the brain are most closely associated with its reinforcing (i.e., pleasurable) and other behavioral effects. The initial site of the pleasurable effects may be the dopamine transporter of mesolimbocortical neurons. Cocaine action at the dopamine transporter inhibits dopamine reuptake, resulting in higher levels of dopamine at the synapse. These pathways may mediate the reinforcing effects of other stimulants and opiates as well. A substantial body of evidence suggests that dopamine plays a major role in mediating cocaine's reinforcing effects, although it is clear that cocaine affects not only the dopamine but also the serotonin and norepinephrine systems.

TOXICITY

In addition to blocking the reuptake of several neurotransmitters, cocaine use results in central nervous system stimulation and local anesthesia. This latter effect may be responsible for the neural and myocardial depression seen after taking large doses. Cocaine use has been implicated in a broad range of medical complications covering virtually every one of the body's organ systems. At low doses cocaine causes increases in heart rate, blood pressure, respiration, and body temperature. There have been suggestions that cocaine's physiologic effects can interact with ongoing behavior, resulting in increased toxicity, such as the additive effects on elevated body temperature of cocaine itself and the increased exertion caused by cocaine. Cocaine intoxication has been associated with cardiovascular toxicity, including heart attacks, stroke, vasospasm, and cardiac arrhythmias.

Cocaine users generally binge, repeatedly, for several hours or days, then follow this with a period in which none is taken. When cocaine is taken repeatedly, chronic intoxication can cause a psychosis, characterized by paranoia, anxiety, a stereotyped repetitive behavior pattern, and vivid visual, auditory, and tactile hallucinations. Less severe behavioral reactions to repeated cocaine use include irritability, hypervigilance (a state of increased sensory awareness of potential threats), suspiciousness, hyperactivity, and eating and sleep disturbances. In addition, when a cocaine binge ceases, users experience a crash, characterized by depression, fatigue, and eating and sleep disturbances. Initially, little cocaine craving accompanies the crash, but as time increases since the last dose of cocaine, users think of little else but the next dose.

Several studies have shown that although initially cocaine increases the neurotransmitters dopamine, serotonin, and norepinephrine, chronic cocaine use reduces function of these neurotransmitters. Positron emission tomography (PET) studies in human cocaine users show a reduction in dopamine release and dopamine receptor availability. These changes are seen for weeks after cocaine use is discontinued, showing that chronic cocaine use can produce long-lasting changes. It is possible that some of the cognitive deficits seen in chronic cocaine users (described in detail below) are related at least in part to these long-lasting changes in neurotransmitter function.

In addition to functional imaging studies in cocaine users, structural imaging studies have also shown evidence of potential neurotoxicity of chronic cocaine use. Magnetic resonance imaging (MRI) studies comparing volumes of specific brain regions between cocaine users and non-drug-using controls have shown that cocaine users have reduced volumes of the prefrontal cortex and increased volumes of caudate and putamen. More recently, studies using

diffusion tensor imaging (DTI) have shown evidence of subtle white matter pathology in cocaine users compared to non-drug using controls. These subtle changes in white matter structure were associated with an increase in a measure of impulsivity, implying that the impulsive behaviors seen in cocaine users may be related to changes in brain structure produced by chronic cocaine use.

BEHAVIORAL EFFECTS

Nonhuman Research Subjects. One of cocaine's characteristics, as a psychomotor stimulant, is its ability to increase the motor behavior of animals. Single low doses produce increases in exploration, locomotion, and grooming. With increasing doses, locomotor activity decreases, and stereotyped behavior patterns (continuous repetitious chains of behavior) emerge. When administered repeatedly, cocaine produces increased levels of locomotor activity, increases in stereotyped behavior, and increases in susceptibility to drug-induced seizures (i.e., *kindling*). This sensitization occurs in a number of different species and has been suggested as a model for psychosis or schizophrenia in humans. Although sensitization to cocaine's unconditioned behavioral effects generally occurs, such effects are related to dose, environmental context, and schedule of cocaine administration. For example, sensitization occurs more readily when dosing is intermittent rather than continuous and when dosing occurs in the same environment as testing.

Learned behaviors, in which animals make responses that have consequences (e.g., press a lever to get food), generally show a rate-dependent effect of cocaine. As with amphetamine, cocaine increases low rates of responding and decreases high rates of responding. Environmental variables and behavioral context can modify this effect. For example, responding maintained by food delivery was decreased by doses of cocaine that either had no effect or increased comparable rates of responding maintained by shock avoidance. Cocaine's effects can also be modified by drug history. Although repeated administration can result in sensitization to cocaine's effects on unlearned behaviors, it generally results in tolerance to cocaine's effects on schedule-controlled responding. This may parallel the tolerance to the pleasurable effects of cocaine seen in humans. This decrease in effect after repeated dosing is influenced by behavioral as well as pharmacological factors.

Human Research Subjects. A major behavioral effect of cocaine in humans is its mood-altering effect, generally believed to be related to its potential for abuse. Traditionally, subjective effects have provided the basis for classifying a substance as having abuse potential, and the subjective effects of cocaine are similar to stimulant drugs of abuse, such as reports of *high*, *liking*, and *euphoria*; increased vigor, friendliness, and stimulation scores; and decreased sedation scores. Subjective effects correlate well with single intravenous or smoked doses of cocaine, peaking soon after administration and dissipating with decreasing plasma concentrations. When cocaine is administered repeatedly, tolerance develops rapidly, so the same dose no longer exerts much of an effect. Users must take increasingly larger amounts of cocaine to achieve the same effect. Tolerance to the cardiovascular effects of cocaine is less complete; there is a potential for the cocaine user to take doses of cocaine that lead to cardiovascular toxicity to try to achieve the euphoric effects of the drug.

Although users claim that their performance is improved by cocaine use, the data do not support their assertions. In general, cocaine has little effect on performance unless performance has deteriorated because of fatigue. Under those conditions cocaine can bring it back to non-fatigue levels. This effect, however, is relatively short-lived, since cocaine has a half-life of less than one hour.

Researchers have studied behavioral effects of chronic cocaine use through a variety of measures, including questionnaires and behavioral laboratory tasks. Using these measures, cocaine dependent individuals demonstrate higher impulsivity and poorer decision-making than non-drug-using control subjects. Some studies have found a correlation between brain imaging findings and behavioral measures in cocaine users, proving that the behavioral changes seen in cocaine-dependent individuals are related to structural or functional changes in their brains. Impulsivity and poor decision-making explain why cocaine dependence is difficult to treat.

TREATMENT

Despite substantial efforts directed toward treatment, cocaine dependence continues to be challenging for

clinicians. As of 2008 the U. S. Food and Drug Administration (FDA) had approved no medications for the treatment of cocaine dependence. However, substantial advances have been made toward improved treatments for this disorder since the late 1990s. At present the mainstay of treatment continues to be non-drug-related. The most effective treatment for reducing cocaine use is a form of behavioral therapy known as contingency management (CM). In CM, patients are given positive reinforcement (such as gift certificates, merchandise, etc.) for providing cocaine-negative urine samples. The main drawback with CM is the difficulty in successfully integrating CM into treatment programs outside research settings, largely due to the cost of the rewards. Another psychological or behavioral treatment that reduces cocaine use is cognitive-behavioral therapy, or CBT; it is often combined with drug therapy in outpatient treatment studies. In CBT, therapists work with the cocaine user to identify and avoid situations and other cues associated with cocaine use.

A number of medications for cocaine dependence were initially successful in open-label trials, but later showed no difference from placebos in controlled trials. Because animal studies show that the rewarding effects of cocaine are mediated by dopamine, several dopamine antagonists have been studied in an attempt to block the rewarding effects of cocaine. Unfortunately, these medications have not proven to be efficacious in placebo-controlled trials. As mentioned above, PET studies demonstrate that chronic cocaine users have lower dopamine release and receptor binding. Consistent with this finding, medications that enhance dopamine function have had more promising results.

A medication that has consistently reduced cocaine use in placebo-controlled trials is disulfiram (Antabuse). Disulfiram is FDA approved for the treatment of alcohol dependence, where it blocks the breakdown of acetaldehye, a noxious alcohol metabolite. Disulfiram also blocks other enzymes that metabolize a range of molecules, including dopamine. Disulfiram's success may be mediated by its effect at inhibiting dopamine beta-hydroxylase, thereby increasing dopamine and reducing norepinephrine concentrations in the brain. Other drugs, such as dextroamphetamine, that worked in at least some placebo-controlled trials also increase dopamine function either directly or indirectly. However, dextroamphetamine can be abused. The wakefulness-promoting medication, modafinil, has a lower abuse potential than dextroamphetamine and has also been effective at reducing cocaine use, possibly by indirectly affecting dopamine through the glutamate system. Other medications that worked in at least one placebo-controlled trial include topiramate and propranolol. Several medications can reduce cocaine use when combined with the behavioral therapy CM, including citalopram, L-dopa, desipramine, and buproprion. The latter three were not effective in clinical trials that did not incorporate CM. Several novel treatments will be studied over the next few years. These include a vaccine that blocks cocaine from getting into the brain as well as pharmacologic agents, such as selective dopamine beta-hydroxylase inhibitors and adenosine antagonists.

In spite of the substantial progress that has been made in development of treatments for cocaine dependence, as yet none have proven effective in the large-scale trials necessary to receive FDA approval. It may well be that different medications will be effective for the various target populations and that variations in dosages and durations of treatment might be required, depending on a variety of patient characteristics. In addition, it is likely that any drug therapy for cocaine dependence will need to be combined with a behavioral intervention to show the greatest efficacy.

See also **Coca/Cocaine, International; Epidemics of Drug Abuse in the United States; Epidemiology of Drug Abuse; Freebasing; Freud and Cocaine; National Survey on Drug Use and Health (NSDUH).**

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CODEINE. Codeine is a natural product found in the opium poppy (*Papaver somniferum*). An alkaloid of opium, codeine can be separated from the other opium alkaloids, purified, and used alone as an analgesic (painkiller). It is however most often used along with mild nonopioid analgesics, such as aspirin, acetominophen, and ibuprofen. These combinations are particularly effective; the presence of the mild analgesics permits far lower codeine doses. Using lower doses of codeine has the advantage of reducing side effects, such as constipation. Codeine is one of the most widely used analgesics for mild to moderate pain.

Structurally, codeine is very similar to morphine, differing only by the presence of a methoxy ($-OCH_3$) group at position 3, instead of morphine's hydroxy ($-OH$) group. The major advantage of codeine is its excellent activity when taken by mouth, unlike many opioid analgesics. Codeine itself has very low affinity for opioid receptors, yet it has significant analgesic potency. In the body, it is metabolized into morphine, and it is believed that the morphine generated from codeine is actually the active agent. Codeine has also been widely used as a cough suppressant. Codeine can be abused, and problems of abuse have often been linked to codeine-containing cough medicines, since they were once easily obtained over the counter. Chronic dosing with high codeine doses will produce tolerance and physical dependence, much like morphine.

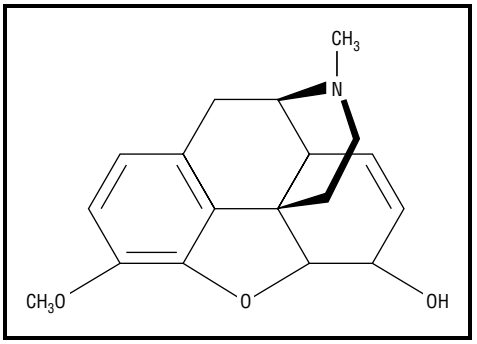

Figure 1. Chemical structure of codeine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Controls: Scheduled Drugs/Drug Schedules, U.S.; Papaver Somniferum.**

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GAVRIL W. PASTERNAK

CODEPENDENCE. The term *codependence* replaced an earlier term, *coalcoholism*, in the early 1970s and achieved widespread acceptance among the general public during the 1980s. Both terms point to problematic beliefs and behaviors that family members of individuals with substance use disorders tend to have in common, and the term *codependence* has been applied to every possible type of addiction.

A rather large non-scientific literature has developed on the topic of codependence. Self-help books addressing codependency (e.g., *Codependent No More*; Beattie, 1987) have sold more than a million copies. Much of the literature is couched in terms of the need to deal with injuries to emotions sustained during childhood—that is, to heal the wounds of the *inner child*, a term popularized by John Bradshaw.

DEFINITION AND CONSTRUCT VALIDITY

Despite the popularity of the concept of codependence in both the general public and among some clinicians, there is a dearth of empirical research on the construct validity of codependence. Furthermore,

a variety of definitions of the construct exist. As noted by Gotham and Sher (1996), codependency has been described as an addiction, a personality disorder, a so-called psychosocial condition, and an interpersonal style.

Potter-Efron and Potter-Efron (1989) define a codependent person as "someone who has been significantly affected in specific ways by current or past involvement in an alcoholic, chemically dependent or other long-term highly stressful family environment" (p. 37). Potter-Efron and Potter-Efron include characteristics of codependency related to both basic personality traits (such as neuroticism) and psychological symptoms (such as anxiety). They described codependents as being affected by involvement with highly stressful family environments. The effects include fear, shame/guilt, prolonged despair, anger, denial, rigidity, impaired identity development, and confusion.

Using Potter-Efron and Potter-Efron's Codependency Assessment Questionnaire (CAQ), Gotham and Sher (1996) assessed the construct validity of codependency. The researchers found that this measure of codependency showed reliability and exhibited a one-dimensional factor structure. However, most of the relation between codependency and family history of alcoholism resulted from general negative affectivity or neuroticism, and there was little in the way of unique information afforded by this measure beyond what one would obtain with more traditional measures of personality.

CHARACTERISTICS

As noted above, codependency has been described in a number of ways. Cermak (1986) described codependency as a personality disorder. Cermak's codependent personality disorder included a number of purported characteristics of codependent individuals. Codependents are thought to have a continued investment of self-esteem in the ability to control both oneself and others in the face of serious adverse consequences. They are thought to exclude their own needs to meet the needs of others. They also are said to experience anxiety and boundary distortions around intimacy and separation. They are enmeshed in relationships with people with psychological disorders, such as personality disorders or substance use disorders. Furthermore, under Cermak's description, codependents have three or more of the following: reliance on denial, constriction of emotions, depression, hypervigilance, compulsions, anxiety, substance abuse, experience of physical or sexual abuse, stress-related medical illnesses, or persistence in a primary relationship with an active substance abuser for at least two years without seeking outside help.

EMPERICAL EVIDENCE OF CODEPENDENCY

Stafford (2001) reviewed proposed definitions of codependency, issues related to the construct validity of codependency, and instruments used to measure codependency. She noted that the myriad definitions and the lack of an operational definition of codependency has been a major impediment to evaluating the utility of codependency as a construct. Furthermore, the author noted that capricious and vague criteria are often included in instruments used to assess codependency and concluded that there is a lack of robust normative data on these instruments. Based on her review, the author advised that professionals should maintain a high degree of skepticism before accepting codependency as a meaningful concept. Other reviewers (Harter, 2000; Sher, 1991) have concluded that there is little empirical evidence for specific syndromes attributed to being a family member of an alcoholic in the literature on adult children of alcoholics (ACOA) and codependence.

However, in 2008, it may be premature to discount the concept of codependence entirely. Lyon and Greenberg (1991) tested the theory that women with an alcoholic parent would be more helpful and more attracted to a man who was portrayed as exploitive than to a man who was portrayed in a more socially desirable manner. Codependent participants (defined as female children of at least one alcoholic parent) and control participants were led to believe that a male experimenter was either nurturant or exploitive. Results suggested that female offspring of an alcoholic parent offered more help to an experimenter presented as exploitive compared to an experimenter presented as nurturant. Furthermore, on self-reported measure of attitudes towards parents, codependents rated their alcoholic fathers more favorably than their mothers and more favorably than the control group rated their nonalcoholic fathers. Thus, according to the authors, codependents appear to maintain positive regard for their alcoholic parent

and are seemingly willing to help exploitive others outside the family environment. However, it is important to note that the codependent group evinced greater self-reported depression than the control group, and thus depression was confounded with codependency to some extent.

Although codependence and related concepts appear to have been embraced by a number of people in the general public and the addiction treatment community, there is little consensus as to what is meant by the term and limited support for various measures purported to assess key components of the concept. Clearly, the family members of alcoholics and other addicted individuals are exposed to a wide range of stressors both inside and outside the home. Moreover, they are likely to experience a range of behavioral problems likely owing to both a problematic home environment as well as genetic liabilities shared with the addicted relative (in the case of children and other biological relatives; Sher 1991). Thus, skepticism over the concept of codependence should not be equated with skepticism over the very real difficulties of individuals who grow up in or live in alcoholic homes. However, it may be better to frame these difficulties within established psychiatric nomenclature (e.g., adjustment disorders, mood disorders, substance use disorders, personality disorders) rather than positing a unique type of disorder that is specific to growing up with or living with an addict.

See also **Adult Children of Alcoholics (ACOA); Al-Anon; Alateen; Families and Drug Use.**

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COERCED TREATMENT FOR SUBSTANCE OFFENDERS.

The issue of mandating or coercing offenders into treatment has been controversial in the past, but as of 2008 is becoming less contentious as evidence accumulates that demonstrates its effectiveness. Originally, treatment advocates maintained that it was an abuse of civil rights to force anyone, even a convicted felon, into unwanted treatment. While this claim might be true for the ordinary citizen, proponents of coercion maintained that those with a history of interrelated substance abuse and criminal activity had lost their right to such considerations. More to the point, some suggested that linkages between criminal and substance abusing behavior paved the way for serious re-consideration of whether offenders had already forfeited their civil rights by violating laws that resulted in the loss of freedom (through imprisonment) or the imposition of constraints while in the community. Others maintained that the state had both a duty and a right to insist that offenders take measures to reduce the likelihood that such behavior would recur in the future.

HISTORY OF COERCION INTO TREATMENT

Coercion of offenders into treatment began in the 1930s with the construction of two federal *farms* in Lexington, Kentucky, and Fort Worth, Texas. The farms were later called *hospitals* and were developed primarily for federal prisoners in need of drug abuse treatment. Volunteers into treatment were also accepted. However, most volunteers left without community follow-up after withdrawal from drugs. Perhaps not surprisingly, relapse was high. As of 2008 most treatment professionals distinguish

between withdrawal from drugs or alcohol, and actual treatment. Treatment for withdrawal (lasting a few days) is not viewed as treatment for substance abuse, which typically lasts from weeks to months and in some cases, especially with offenders, for years.

The coerced treatment of substance abusers resulted from frustration over the fact that substance abusers had limited (or no) incentive to seek treatment, which frequently resulted in criminal behavior. Coercion into treatment was seen as a means of reducing arrests, crime, and drug use. From the criminal justice perspective, drug use was—and is—forbidden, although from a public health harm reduction perspective, reduced drug use was viewed as a positive achievement. Although coerced treatment for substance abuse was traditionally associated with community treatment, it eventually became an important component of the justice system and its approach to offenders with a substance abuse history.

NARCOTIC ADDICT REHABILITATION ACT

In 1966, the Narcotic Addict Rehabilitation Act (NARA), based on New York and California civil commitment coerced treatment models, was enacted by Congress as a federal civil commitment program to reduce drug use. Court-ordered treatment was initially provided at the Lexington and Fort Worth hospitals. Subsequently, in-patient treatment facilities were opened in several cities and served as the foundation for community-based drug abuse treatment. When NARA was phased out, the U.S. Public Health Service facilities were transferred to the Federal Bureau of Prisons in the mid-seventies (Leukefeld & Tims, 1988, pp. 236–251).

TREATMENT ACCOUNTABILITY FOR SAFER COMMUNITIES (TASC)

In the 1970s, prison-based programs such as Cornerstone in Oregon and Stay 'n' Out in New York State gained a reputation for successful treatment of inmate substance abusers. Another well-known program associated with coerced substance abuse treatment was the Treatment Alternatives to Street Crime (TASC) program, later called Treatment Accountability for Safer Communities. TASC was based originally in New York City and Washington, DC, although as of 2008 the association had established more than two hundred programs throughout the United States. TASC made a critical contribution to the justice and treatment delivery systems by emphasizing the importance of strengthening linkages between the two systems. Previously, criminal justice practitioners tended to view treatment as too soft an approach for criminals, while treatment professionals viewed the justice system as too rigid. In addition, for years treatment advocates maintained that substance abusers needed to hit bottom and want treatment, in order for treatment to be successful. The justice system, by contrast, felt that society at large could not afford to wait until substance abusers hit bottom or wanted to be treated. Eventually, however, the two systems learned to collaborate, with rewarding and impressive results.

Although effectiveness of treatment could be measured in several ways, in the context of treatment for substance abusing offenders, many agreed that appropriate goals were reductions in criminal and substance abuse behaviors following treatment. Thus, it was important to study the post-treatment outcomes of such offenders to determine whether they refrained from future crime or substance abuse.

Beginning in the mid-eighties, evidence began to mount which suggested that, in fact, coerced treatment for offenders with a history of substance abuse was associated with reductions in both drug/alcohol use and criminal activity (Wexler et al., 1992, pp. 156–175).

In the late nineties, researchers conducted coordinated studies at three prison-based substance abuse treatment programs in California, Delaware, and Texas, to test the effectiveness of adding an aftercare component to their programs. Although these three programs were located in different geographical regions, in different states and with different (though comparable) populations, research findings were virtually the same: The aftercare component increased the effectiveness of the three treatment programs. Simply put, those offenders who had completed treatment did better (in terms of drug use or criminal arrests after release from prison and treatment) than those who had not received treatment. In addition, those who had completed treatment and received aftercare did better than those who completed treatment but did not receive aftercare (Knight et al., 1999, pp. 337–351; Martin

et al., 1999, pp. 294–320; Wexler et al., 1999, pp. 321–336).

These studies appeared to confirm the cost effectiveness of both treatment and aftercare, confirming findings of earlier research (CALDATA, 1994, p. 89) that reported that for every dollar spent on treatment, the state benefited sevenfold. By the beginning of the new millennium, additional research suggested that treatment for substance offenders was cost effective (Aos et al., 2001; McCollister et al., 2003). These findings were important in responding to questions raised by those who wondered whether treatment for offenders was ultimately cost effective. But researchers warned that findings should be interpreted with caution because offenders might have entered treatment voluntarily rather than because it was mandated. However, imprisoned offenders have very few choices, and to that extent they are already in a state of coercion.

MOTIVATIONAL READINESS FOR TREATMENT

The issue of motivational readiness for treatment has been cited as a problem for those mandated to treatment. Clearly, whether offenders are motivated to seek treatment has implications for how receptive they may be to such treatment. Clinicians have developed training to address this issue. Motivational training for treatment has gained recognition as a method for facilitating entry into treatment for substance abuse by those who may otherwise resist such treatment.

DRUG TREATMENT ALTERNATIVE-TO-PRISON (DTAP)

In 2003, a White Paper published by the National Center on Addiction and Substance Abuse at Columbia University (CASA) reported findings from its evaluation of the Drug Treatment Alternative-to-Prison (DTAP) program based in Brooklyn, New York. Although the DTAP program was originally a kind of diversion program for prisoners charged with drug crimes, the program was changed to a deferred sentencing model. This meant that participants who pled guilty to a felony might enter treatment as an alternative to prison but that program violations would immediately result in punishment and imprisonment.

The CASA evaluation found that DTAP graduates had re-arrest rates that were 33 percent less than those of the matched comparison group two years following treatment; reconviction rates were 45 percent less. In addition, DTAP graduates were three and one-half times more likely to be employed than they were prior to incarceration. (Ninety-two percent were employed following graduation from DTAP, compared to only 26 percent who were employed prior to incarceration.) Findings for non-graduate participants in the program were more impressive also than for non-participants.

CASA calculations were that DTAP costs were substantially less than the costs for ordinary imprisonment ($64,338); the average cost of residential drug treatment, vocational training, and support services for a DTAP participant was $32,975, barely more than half the cost of imprisonment.

See also **Prisons and Jails, Drug Treatment in; Shock Incarceration and Boot-Camp Prisons; Treatment, Stages/Phases of: Aftercare.**

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COFFEE. Coffee is the world's most common source of caffeine, providing a little more than half of all caffeine consumed daily. In the United States, coffee is usually a beverage made by percolation or infusion from the roasted and ground or pounded seeds of the coffee tree (genus *Coffea*), a large evergreen shrub or small tree, which was native to Africa but now is grown widely in warm regions for commercial crops. Caffeine from coffee accounts for an estimated 125 milligrams of the 211 milligrams of U.S. caffeine consumed per capita per day. Recent estimates suggest that more than 50 percent of the adolescents and adults in the United States consume some type of coffee beverage. Coffee is one of the main natural commodities in international trade, ranking second only to petroleum in dollar value. Approximately fifty countries export coffee and virtually all of those countries rely on it as a major source of foreign exchange. An estimated 25 million people make their living in the production and distribution of coffee products.

In addition to caffeine, roasted coffee contains at least 610 other chemical substances, which may contribute to its smell, taste, and physiological effects.

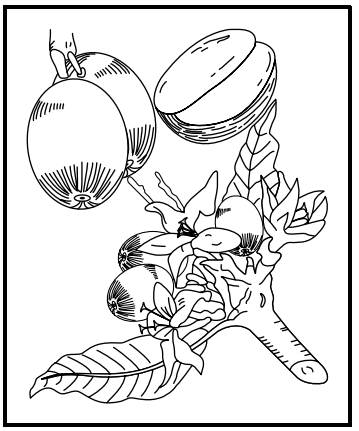

Figure 1. Coffee plant. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Nevertheless, coffee's primary psychoactive ingredient is caffeine. The amount of caffeine in an individual cup of coffee varies considerably, depending on the type and amount of coffee used, the form of the final coffee product (e.g., ground roasted or instant), and the method and length of brewing. On average, a 6-ounce (177 milliliters) cup of ground roasted coffee contains about 100 milligrams caffeine; the same amount of instant coffee typically contains about 70 milligrams caffeine. However, the caffeine content of any given 6-ounce cup of coffee can vary considerably and can reach as much as 210 milligrams. Drip coffee typically contains more caffeine than percolated; decaffeinated coffee contains a small amount of caffeine, approximately 4 milligrams in a 6-ounce cup. Individual servings of caffeinated coffee contain amounts of caffeine that have been shown experimentally to produce a range of effects in humans including the alteration of mood and performance and the development of physical dependence with chronic daily use.

Coffee cultivation probably began around 600 CE in Ethiopia, but the drink was spread into the Middle East and Europe. Today, much of the world's coffee is grown in South and Central America, particularly Brazil and Colombia, and in several African countries. Coffee beverages derive primarily from the seeds of two species of *Coffea* plants, *Coffea arabica* and *Coffea canephora* var. *robusta*. Robusta coffees contain approximately twice as much caffeine as Arabicas. Arabica beans are used in the majority of the coffee consumed today, particularly in the higher quality coffees. Since processing for instant and decaffeinated coffee extracts flavor components from the bean, the stronger flavored beans, typically Robusta beans, are used for these coffee products. Caffeine extracted in the decaffeination process is sold for use in soft drinks and medications.

The coffee bean, covered with several layers of skin and pulp, occupies the center of the coffee berry. During the first part of coffee production, the outer layers of the coffee berry are removed, leaving a green coffee bean. The beans are then roasted, removing between 14 and 20 percent of their water and changing their color from green to various shades of brown; generally, the beans get darker as more water is extracted. The beans are then ground and ready for use. To produce instant coffee, roasted and ground coffee is percolated to produce an aqueous coffee extract. That extract is dehydrated by spray or freeze-drying to produce water-soluble coffee extract solids. Since this process removes flavor and aroma from the coffee, compounds are added to the extracts at the completion of the process to restore the lost characteristics.

See also **Caffeine; Colombia.**

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COLA/COLA DRINKS. Cola drinks are carbonated soft drinks that contain some extract of the kola nut in their syrup. Kola nuts are the chestnut-sized and -colored seeds of the African kola tree (*Cola nitida* or *Cola acuminata*). For the soft-drink industry, the trees are, as of 2008, grown on plantations throughout the tropics. Historically, kola nuts were valued highly among African societies for their stimulating properties. Kola nuts were cracked into small pieces and chewed for the effect, which increased energy and elevated mood in extremes of heat, hunger, exhaustion, and the like. European colonists in Africa learned of the effect and some chewed the nuts. In the 1800s, Europeans brought kola nuts to various strenuous endeavors in Africa and in other regions, and they began to increase the areas under cultivation. Kola nuts were soon finely powdered and made into syrups for ease of use, with no loss of effect, it was claimed.

The active ingredient responsible for these stimulatory properties is caffeine, a powerful brain stimulant, which is also present in other plants such as coffee, cocoa, tea, and maté. Besides reversing drowsiness and fatigue, a heightened awareness of stimuli and surroundings may occur. Studies have shown that less energy may be expended by the

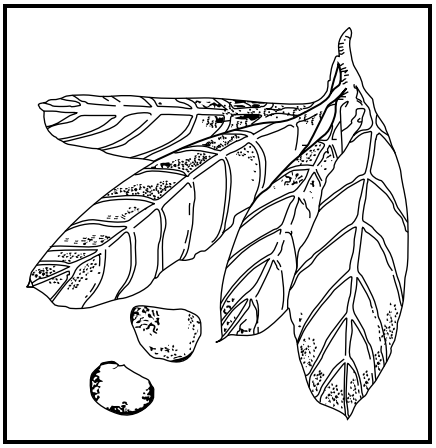

Figure 1. Kola leaf. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

musculature with equal or greater results—in animals as well as humans—but excess use causes tolerance and dependence, often unrealized until deprivation results in severe headaches. Large doses can cause nervous irritation, shaking, sleep disturbances, insomnia, and aggravation of stomach ulcers or high blood pressure.

In the late 1800s, in the United States, cola drinks came onto the market with other carbonated or phosphated (fizzy) drinks. Coca-Cola, one of the first and most popular, contained extracts of both the coca plant (cocaine) and the kola nut (caffeine), but by the early 1900s, with the realization of its dangers, cocaine was removed and replaced by additional caffeine and a decocainized extract. Drinking cola is common in the United States and emulated worldwide, with many brands competing for a huge and growing consumer market. As of 2008, colas were available with sugar or artificial sweeteners, with or without caffeine, with or without caramel coloring (clear), thus indicating that people seem to like the flavor regardless of the specific ingredients or the effect.

David Courtwright's historical study of the origins of the worldwide use of kola points out that the makers of Coca-Cola faced litigation in the United States as early as 1911 on the grounds that the caffeine in the drink was habit-forming and an unlabeled additive in a product advertised to children and adults alike. The result of the trial forced Coca-Cola to reduce caffeine amounts by half, but by then the product was available throughout the United States. During World War II, American soldiers introduced Coke to Europe and Japan, and dozens of bottling plants were built immediately after the war ended. By 1991, Coke was available in 155 nations.

Despite the truthful claims by soft-drink companies of responsible improvements to their products by removing kola extract, caffeine remains the key psychoactive ingredient of these soft drinks. Courtwright argues that products such as Coca-Cola are not only stimulating drugs, but cultural and political symbols that never would have become so in the absence of caffeine or a like stimulant.

Several medical studies conducted in the late-twentieth century linked the consumption of cola drinks by physically active adolescent girls to increased bone fractures as compared to those who abstained from colas. A Harvard University School of Public Health study could not determine the exact cause, but speculated that phosphoric acid contained in cola drinks adversely affects calcium metabolism and bone mass. Coupled with the belief that many teens replace milk with soda in their diets increased the likelihood of a decrease in bone density. In addition, research indicates that adolescents who consume excessive amounts of colas (1.5 liters per day or eleven liters per week) or other caffeinated beverages experience daily or near–daily headaches. Public health officials have also noted a dramatic increase in calorie consumption among adolescent cola drinkers.

Phosphoric acid in cola has also been linked to weakened bone density in older women. A 2006 Tufts University study found that regular consumers of cola drinks were likelier to experience decreased bone mineral density in the hip. Such a decrease could lead to osteoporosis and, ultimately, fractures of the hip that are often debilitating or even fatal among older women. However, critics of the 2006 study noted that while the corollaries between phosphoric acid in cola and bone deterioration are quite plausible, research comparing bone loss over time between cola drinkers and non-cola drinkers is necessary to confirm a connection.

See also **Caffeine; Coca Paste; Coca Plant.**

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REVISED BY MATTHEW MAY (2009)

COLLEGE ON PROBLEMS OF DRUG DEPENDENCE (CPDD), INC.

The College on Problems of Drug Dependence (Martin W. Adler, Ph.D., Executive Officer, CPDD, Department of Pharmacology, 3420 N. Broad Street, Philadelphia, PA 19140; http://views.vcu.edu/cpdd/) is the nation's oldest organization devoted to the problem of drug use and addiction. It is an incorporated, not-for-profit, scientific organization that acts independently of both the U.S. government and the pharmaceutical industry while fostering an exchange of knowledge and resources across the academic, medical, governmental, and business communities. The CPDD is known internationally as a World Health Organization Collaborating Center for research and training in the field of drug dependence. The CPDD also offers consulting services and, along with the National Institute on Drug Abuse, supports drug-dependence testing and research at several select U.S. universities.

Among the goals of the CPDD are the following:

1. to support, promote, and carry out abuse-liability research and testing, both at the preclinical and clinical levels;
2. to serve as advisor to both the public and private sectors, nationally and internationally;
3. to sponsor an annual scientific meeting in fields related to drug abuse and chemical dependence.

The annual scientific meeting of the CPDD has become one of the few forums where scientists from diverse disciplines can discuss problems of drug abuse and drug dependence at a rigorous academic and scientific level.

A primary goal of the CPDD is the publication of data on the physical-dependence potential and abuse liability of opioids, stimulants, and depressants, as well as the development of a new methodology for drug evaluation. These data provide an independent scientific evaluation of drugs that might have abuse liability. A number of scientists from various medical schools work collaboratively to assess these drugs. The data are collated in the Laboratory of Medicinal Chemistry, National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Bethesda, MD. They are discussed by the Drug Evaluation Committee of the CPDD before publication. Government agencies can use the data to help determine whether a medically useful drug should be scheduled under the Controlled Substances Act to restrict access and thus reduce possible abuse.

The contemporary CPDD originated in 1913, as the Committee on Drug Addiction of the Bureau of Social Hygiene in New York City. In 1928, the Bureau of Social Hygiene provided funds to the Division of Medical Sciences, National Research Council (NRC), of the National Academy of Sciences (NAS), for the support of a chemical, pharmacological, and clinical investigation of narcotic drugs by the Committee on Drug Addiction, NRC, NAS. This research continued until World War II. From 1939 to 1947, the Committee on Drug Addiction served as an advisory group to the U.S. Public Health Service (Eddy, 1973).

The Committee on Drug Addiction was reestablished in 1947 as the Committee on Drug Addiction and Narcotics (CDAN), in the Division of Medical Sciences of the NRC, NAS. In 1965, CDAN's name was changed to the Committee on Problems of Drug Dependence (CPDD). The CPDD remained as an NRC, NAS committee until 1976, when it became an independent scientific organization, the Committee on Problems of Drug Dependence (CPDD), Inc. It was guided by a

Board of Directors with the sponsorship of nine major scientific organizations (May & Jacobson, 1989). In 1991, the CPDD underwent its most recent reorganization and its name was modified to reflect its contemporary role. Now known as the College on Problems of Drug Dependence, Inc., the CPDD has become a scientific membership organization that enables its members to have a voice on issues relating to drug abuse. Sixteen institutions and professional and scientific societies are affiliated with or have liaison representation with the CPDD, including such diverse groups as the American Chemical Society, the American Medical Association, and the Food and Drug Administration.

The members of the CPDD are involved in all the aspects of the effects of drugs subject to abuse—encompassing the enormous range from social, economic, and political issues through basic research in molecular biology and the study of the interaction of these drugs with specific receptors in the central nervous system. Membership is divided into four categories: Fellows, Regular Members, Associate Members, and Student Members. In addition, corporations with an interest in the field may join as Corporate Members. The CPDD sponsors the publication of the monthly journal, *Drug and Alcohol Dependence*, an international journal covering the scientific, epidemiological, sociological, economic, and political aspects of substance abuse.

See also **Drug Types; World Health Organization Expert Committee on Drug Dependence.**

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COLOMBIA. Colombia's role in illicit drug production and trafficking has evolved over the past several decades. Colombia is the only country where three plant-based illegal drugs—marijuana, cocaine, and heroin—are produced. Drug trafficking has played a major role in Colombia's history for the past 30 years, profoundly impacting Colombian democratic institutions, the ongoing civil conflict, and its environment. Definitively explaining why Colombia's illicit economies have played such a central role is impossible. Many analysts point to Colombian geography; the country has both Atlantic and Pacific coastlines, large jungle areas with little or no state presence, and relatively unpoliced borders. Black markets also have deep roots in Colombian political culture and institutions, and the country has a long history of smuggling, contraband, and corruption. Drug production and trafficking methods have evolved in response to changing counternarcotics policies, primarily programs established and funded by the U.S. government. Colombia does not have a major tradition of indigenous ritual drug consumption, with only a few small indigenous groups (making up less than 2% of the total population) regularly using coca and hallucinogenic plants for religious and medicinal reasons. Nonindigenous Colombians have historically low rates of illicit consumption.

Determining the full extent of drug production and trafficking is impossible, given the serious problems with existing data and statistics, which are often estimates driven by political agendas. In part, these difficulties are the result of the nature of illicit economies; because these activities are illegal, they are hidden and thus inherently difficult to quantify. In addition, many of the statistics describing the illicit drug trade are methodologically unsound and ideologically driven (Thoumi, 2005). The United Nations and various U.S. drug enforcement agencies often produce varying statistics, in part because of the technological and methodological differences in their measurement, for example, in estimating Colombian coca cultivation (including overflights versus satellite photography, and the degree of small-scale sampling). There have been significant disagreements over the estimates of the role of illegal armed groups in the drug trade (see below). Figures about the Colombian drug trade vary widely depending on the source. During the 1980s and 1990s the drug trade was widely described as contributing significantly to Colombia's economic stability during the era's debt crisis; this was later disputed by some Colombian

economists, who estimated that the amount of money entering the national economy was less than originally believed. The illicit economy did indisputably impact regional economies, such as the cities of Medellin and Cali and other smaller periodic hubs of drug production and trafficking. These areas have clearly experienced boom-bust cycles, with drug trade profits fueling construction and other economic activity. Such economic activity has not, however, led to longer-term financial stability in these areas. These boom-bust cycles distort local economies rather than provide the basis for long-term investment. The state is unable to capture resources through taxation to invest in infrastructure and public services. Some scholars argue that although the illicit economy has played a smaller role in Colombia's overall economy since the 1990s, the damage done by the black market has increased because of its long-term impact and the role drug trafficking has assumed in sustaining illegal armed groups (Thoumi, 2003).

Colombian counternarcotics policies are profoundly influenced by U.S. policies; the United States provides significant funding for these programs. Since 1989 the U.S. government has defined drug trafficking as a national security threat, so its counternarcotics programs abroad aim to lower the amount of illicit drugs entering the United States. In Colombia, such programs have additional objectives as part of counterinsurgency and, since 9/11, counterterrorism programs, as the U.S. and Colombian governments intend to deny insurgent groups resources derived from the illicit drug trade.

Counternarcotics efforts include legal restrictions on precursor chemicals to prevent drug manufacturing, financial laws to limit money laundering, eradication (the destruction of plant crops), and interdiction to interrupt trafficking routes. Eradication to destroy marijuana, coca, and opium poppy plants can be voluntary, usually done by hand by farmers themselves, often in exchange for social services and technical support for transitioning to legal agricultural crops, known as alternative development or crop substitution programs. Forced eradication can involve manual eradication carried out by military or police forces, or through fumigation, the aerial spraying of chemical herbicides. Fumigation first began in Colombia in the 1970s, targeting marijuana plants. Large-scale fumigation operations began to target coca crops in southern Colombia in the late 1990s. Peasant farmers in these areas allege that spraying causes health problems, and destroys legal crops and livestock, as well as negatively impacting the watershed and ecological diversity; government officials claim that coca cultivation itself is more ecologically damaging and that no definitive health effects have been proven.

In the 1970s a boom in marijuana cultivation along Colombia's Atlantic coast created a class of newly rich traffickers supplying the U.S. market. Large maritime vessels carried bulk shipments of marijuana to prearranged points off the U.S. coast. Law enforcement efforts spearheaded by the U.S. Drug Enforcement Administration (DEA) shut down these trafficking routes.

Colombia first became significantly involved in the cocaine trade as a site for refining and trafficking beginning in the late 1970s, when coca paste produced in Peru and Bolivia was brought there for processing and then shipped to the United States. In the early twenty-first century the cultivation of coca has expanded enormously in Colombia. Unlike in Peru and Bolivia, where peasants have for centuries grown and chewed the coca leaf (a mild stimulant, compared with its processed form, cocaine), in Colombia this practice is limited to a very few, small indigenous groups.

Colombia's well-publicized cartels, first in Medellin and then Cali, expanded from marijuana to the processing and export of cocaine. A small number of powerful drug kingpins, including Carlos Lehder-Rivas, Jorge Ochoa, Pablo Escobar, Griselda Blanco, Jose Rodriguez-Gacha, and the Herrera brothers, came to control a billion-dollar cocaine industry that processed coca grown primarily in Bolivia and Peru. As cocaine and then crack became more popular within the United States, the cartels developed new forms of trafficking, including the use of mules (individuals paid to transport drugs by ingesting them; this practice is extremely dangerous because of possibility of detection as well as death if the protective sealant ruptures). Air-dropping involves parachuting waterproof containers of drugs into the ocean from low-flying planes off the coast of Florida. These containers are then picked up by boats and brought ashore as a means of escaping radar detection. Traffickers

also frequently smuggle narcotics within legal shipments of commercial goods, relying on high profit margins to offset the small percentage of such shipments that are confiscated by customs officials. Each new innovation requires law enforcement officials to develop new detection methods.

Colombia first began producing opium poppies for heroin in 1986; by 2003 there were approximately 4,000 hectares in production supplying consumers in the eastern United States and Europe. Poppies are grown in higher altitudes, primarily the southwestern mountains, making eradication efforts more difficult.

IMPACT ON DEMOCRACY

The power and violence of the drug industry have had a profound impact on Colombia's democratic institutions, as signified by the expression *plata o plomo*—silver or lead—meaning "take the bribe or take a bullet." Drug lords achieved significant political influence through threats, bribery, and political contributions. In the early 1980s Pablo Escobar was elected as a congressional alternate, this being the most visible effort of drug traffickers to co-opt the electoral process. Later in the same decade the Medellin cartel waged war on the Colombian government, killing hundreds of judges, police investigators, journalists, and public figures. The killing of a major public figure became known as *magnicidio* (from the word for murder, *homicidio*); those assassinated by drug traffickers included Minister of Justice Rodrigo Lara Bonilla (in 1984) and presidential frontrunner Luis Carlos Galan (in 1989).

Some U.S. officials were led to refer to Colombia as a "narcostate" during the administration of President Ernesto Samper (1994–1998) when the DEA released evidence that his campaign had accepted contributions from the Cali cartel, resulting in a large investigation implicating a number of politicians and generating an ongoing crisis for his administration. Gunmen linked to the drug trade regularly attacked judicial investigators, judges, and prosecutors, contributing to the weakening of the Colombian legal system and a larger crisis in the rule of law. In 2008 the so-called *para-politica* scandal erupted when investigative journalists uncovered relationships between drug-trafficking paramilitaries and hundreds of public officials, including members of Congress, governors, mayors, and other local politicians.

DRUGS AND CONFLICT

Although the vast majority of Colombian violence is attributed to common crime, much of this violence is believed to be related to the drug trade. During the 1980s and 1990s Colombia had one of the highest homicide rates in the world. Colombia is also home to the longest-running internal conflict in the hemisphere, the partisan political conflict of the 1950s that was reborn as the Marxist guerrilla insurgencies of the 1960s and 1970s. Scholars and politicians continue to debate the role of the illicit narcotics trade in the conflict; throughout the 1980s and 1990s many insisted that the primary reason for the conflict was political and ideological. Following his election as president in 1998, Alvaro Uribe (2002–2010) refused to acknowledge Colombia as a country in conflict, instead insisting that "if Colombia would not have drugs, it would not have terrorists." All analysts agree that the profits from the illegal drug trade have shifted the dynamic of violent conflict, allowing armed groups to become self-financing, limit their reliance on public support, and expand their military strength into new areas.

Guerrilla groups active in areas of coca cultivation, primarily the Revolutionary Armed Forces of Colombia (Fuerzas Armadas Revolucionarias de Colombia or FARC), have increasingly financed their activities by taxing coca crops and by protecting drug processing labs and other illicit installations. While coca cultivation declined in the 1990s in Peru and Bolivia due in part to U.S.-financed eradication programs, cultivation in Colombia increased, leaving overall Andean coca production constant. Although coca production in Colombia in 1991 accounted for approximately 13 percent of the world's total production, by the end of the 1990s that number had increased to 75 percent. The dramatic increase in coca cultivation in southern Colombia, a FARC stronghold since the 1960s, coincided with the organization's strategic effort to increase its military capabilities in the mid-1990s. U.S. State Department officials have used the arrests of individuals allegedly linked with FARC in Mexico and Brazil to bolster their claims that FARC members are "narcoguerrillas" and that Colombia's drug cartels and guerrillas are completely integrated. The United States did extradite two senior FARC leaders for their role in drug trafficking, but these trials resulted in initial verdicts of not guilty. Many scholars argue that historically FARC has been involved only minimally in

the illicit industry's most lucrative stages: transshipment and sale of drugs on the international market. Evidence of the group's growing criminalization continues to increase, however.

Right-wing paramilitary groups reached the height of their power in the middle of the first decade of the twenty-first century. In the 1980s, money from the drug trade allowed paramilitary death squads to grow from small groups linked to local military commanders to private armies. The fusion of counterinsurgency ideology and illegal narcotics revenue produced one of the most lethal fighting forces in Latin America. As the owners of vast haciendas (the result of money laundering and efforts to buy their way into the landed gentry, known as *reverse agrarian reform*), drug traffickers needed protection from guerrilla kidnapping and extortion. Paramilitary groups linked to drug cartels (particularly the Medellin cartel) worked closely with Colombian military officers to eliminate suspected guerrilla sympathizers, while at the same time they attacked Colombian authorities who were attempting to investigate drug trafficking. In 1997 paramilitary spokesmen announced the creation of a national coordinating body of paramilitary groups, the United Self-Defense Forces of Colombia (Autodefensas Unidas de Colombia or AUC). Newly created mobile squads carried out numerous massacres as paramilitary forces moved to control new areas of the country. In 2003 the government began a demobilization program targeting these groups; critics of the process have demonstrated that many groups remain significantly involved in drug trafficking. Dozens of paramilitary leaders have been extradited to the United States to face drug trafficking charges.

COUNTERNARCOTICS POLICIES IN COLOMBIA

Beginning in 1989 with the so-called Andean strategy, U.S. funds, equipment, and logistical support, and personnel from the DEA, the CIA, and other agencies have played a leading role in counternarcotics operations in Colombia. U.S.-assisted operations resulted in the killing of Pablo Escobar in 1993 and the jailing of the heads of the Cali cartel in 1994. However, the breakup of the two largest cartels did not lead to a long-term decline in Colombian drug trafficking. These drug syndicates have since been replaced by smaller, more vertically integrated trafficking organizations—often called *baby cartels*—whose nimble, independent traffickers are much more difficult to detect and infiltrate. These traffickers employ new and constantly changing shipping routes through Central America, Mexico, and the Caribbean and increasingly through Africa, for moving cocaine and, increasingly, heroin.

First passed by Congress in 2000, the U.S. assistance package known as Plan Colombia shifted the bulk of counternarcotics assistance to the Colombian Army. Although Colombian President Andrés Pastrana's original Plan Colombia (1998) presented a four-pronged strategy to support efforts for peace, development, political reform, and citizen security, U.S. assistance has been massively skewed toward militarized counternarcotics operations. Described as an "emergency" supplemental package, President Bill Clinton's $1.3 billion program made Colombia the third largest recipient of U.S. security assistance in the world at that time. The centerpiece of the proposal was $600 million to support Colombian Army operations in the FARC stronghold of southern Colombia. This funding trained and equipped new Colombian Army counternarcotics battalions by providing them with helicopters, transport, and intelligence assistance. The package also devoted significant resources to development, rule of law, and human rights programs. Since then subsequent yearly appropriations have maintained funding levels between $700 million and $1 billion; in 2008 the funding appropriation shifted to increase the balance between military and nonmilitary spending.

The drug trade in Colombia continues to evolve. FARC has been hard hit by government counterinsurgency programs, with a number of high-profile desertions and commanders killed in combat. Analysts predict that many regional fronts may deepen their involvement in criminal activities, including illicit drug production and trafficking. Despite the official demobilization of AUC, paramilitary control structures persist in many areas of the country and analysts believe that their central role in drug trafficking will continue as well. Coca cultivation in Colombia has spread from its southern jungles to other regions throughout the nation: along the Venezuelan border and Pacific coast, and in the southern Magdalena Valley region.

See also **Crop Control Policies; Drug Interdiction; Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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WINIFRED TATE

COMPLICATIONS

This entry includes the following essays:

MEDICAL AND BEHAVIORAL TOXICITY OVERVIEW

Alcohol and other drugs of abuse cause considerable adverse health effects. Both legal and illegal drugs (substances) of abuse are taken to modify mood, feeling, thinking, and perception. As with most drugs (medications), both acute and chronic toxicities occur. In general, the term *acute* refers to the short period of time when the drug is present in the body, exerting its main effects. The term *chronic* refers to a longer period, usually years. Acute toxicity results in the impairment of behavior leading to other complications (e.g., trauma), and in the case of some drugs, high doses can decrease breathing (respiratory depression) or change the rhythm of the heart, leading to accidental or intentional death. Chronic use can result in organ damage, which may lead to chronic illness or death (as with alcoholic cirrhosis of the liver). Persistent use of many classes of drugs also leads to *tolerance* (so that an increased amount of the drug is required to produce the same effects) and physiologic (physical) dependence, so that a withdrawal syndrome is associated with sudden cessation of drug use. Drug users who use hypodermic needles and syringes (injecting drug users [IDUs]) are at risk for blood-borne diseases associated with the use of contaminated equipment, such as Hepatitis B and C and human immunodeficiency virus (HIV 1 and 2, the viruses responsible for acquired immunodeficiency syndrome [AIDS]).

This entry focuses on alcohol as the representative drug, but other drugs of abuse are mentioned when appropriate. In North America, the diagnosis of alcohol and other psychoactive substance abuse/dependence is usually made according to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) of the American Psychiatric Association (APA). The fourth edition, text revision, referred to as *DSM-IV-TR*, defines psychoactive substance dependence as the presence of at least three of the following (within the same 12-month period):

1. tolerance, as defined by either of the following: (a) need for markedly increased amounts of the substance to achieve intoxication or desired effect; (b) markedly diminished effect with continued use of the same amount of the substance
2. withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome for the substance (b) the same (or closely related) substance taken to relieve or avoid withdrawal symptoms
3. the substance is often taken in larger amounts or over a longer period than was intended
4. a persistent desire for or unsuccessful efforts to cut down or control substance use
5. a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain smoking), or recover from its effects
6. important social, occupational, or recreational activities are given up or reduced because of substance use
7. continued substance use despite knowledge of having had a persistent or recurrent physical or psychological problem that was likely to have been caused or exacerbated (worsened) by the

substance (e.g., recurrent cocaine use despite recognition of cocaine-induced depression; continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

The diagnosis of alcohol and other substance abuse (as opposed to dependence) relies on the following:

A maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by one or more of the following occurring at any time during the same 12-month period:

1. recurrent substance use resulting in a failure to fulfill major obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
2. recurrent use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
3. recurrent substance-related legal problems (e.g., multiple arrests for substance-related disorderly conduct)
4. continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with family members about consequences of intoxication; physical fights)

Alternatively, the symptoms have never met criteria for substance dependence for this class of substance.

These criteria continue to evolve, as can be tracked at the Web site maintained by the American Psychiatric Association, and are likely to be changed in the future (progress was under way as of 2008 for the publication of *DSM-V*, which was expected to be published in 2012). Clearly the lack of one of the above diagnoses does not preclude a given person from being at risk for complications of alcohol or drug use (e.g., trauma as a result of intoxication).

ACUTE EFFECTS OF ALCOHOL

At the level of the cell, very high doses of alcohol (ethanol) seem to act by disrupting fat (lipid) structure in the central nervous system (anesthetic effect). Lower doses are thought to interact with various proteins and neurotransmitter receptors, such as glutamate, gamma-amino butyric acid (GABA), glycine, serotonin (e.g., 5HT3), and neuronal nicotinic receptors. Other actions may involve modulation of membrane ion (e.g., calcium) channels. The reinforcing (rewarding) effects of alcohol may be mediated via dopamine (a neurotransmitter) in specific brain regions; dopamine acts as an intermediary compound in the reinforcement process. The reinforcement of responses to other drugs of abuse, such as cocaine, is also thought to be mediated via dopamine.

The acute effects of alcohol are well known. In low doses, it causes blood vessels to dilate, and the skin to become flushed and warm. The individual under the influence of alcohol experiences a feeling of relaxation and mild sedation but may become talkative with loss of inhibitory control of emotions. Small doses (one to two drinks) do not impair complex intellectual ability; however, as the dose increases (two or more drinks or as the blood alcohol concentration approaches and exceeds the legal limit) impairment at multiple levels of the nervous system occurs. All types of motor performance are eventually affected, including maintenance of posture, control of speech, and eye movements. Movement becomes slower and more inaccurate. Mental functioning decreases, such that there is impairment in attention and concentration and a diminishing ability to make mental associations. Concurrently, the ability to attend to incoming sensory information is decreased. Night and color vision are impaired. Judgment and discrimination and the ability to think and reason clearly are adversely affected. Further increased doses result in a stuporous condition associated with sleeping, with vomiting, and little appreciation of surroundings. This level is followed by coma and sometimes death from decreases in the functioning of the brain centers that control respiration.

ACUTE EFFECTS OF OTHER DRUGS OF ABUSE

Other drugs of abuse can be classified into stimulants, depressants, opioids, and drugs that alter perception (including hallucinogens). The effect of any drug depends on the dose taken at any one

time, the previous drug experience of the user, the circumstances in which the drug is taken, and the manner (route of administration) in which the drug is taken.

Stimulants such as cocaine and amphetamine produce euphoria, increased confidence, increased sensory awareness, increased anxiety and suspiciousness, decreased appetite, and a decreased need for sleep. Physiological effects include increases in heart rate, blood pressure, and pupil size, and decreases in skin temperature.

Depressants such as the minor tranquillizers (including the benzodiazepines, barbiturates, and other sedative-hypnotics) produce acute effects of a similar nature to alcohol, which is also a depressant. Actual effects vary according to drug, so that benzodiazepines (such as diazepam [Valium]) produce less drunkenness compared to alcohol or barbiturates. The term *opioid* refers to both drugs derived from opium (opiates) and other synthetic drugs with similar actions, those acting on the same receptor system. The term *narcotic* is usually synonymous with opioid, but it can technically also include other drugs listed in the Harrison Narcotics Act (e.g., cocaine). Opioids produce euphoria, sedation (to which rapid tolerance develops), itching, increased talkativeness, increased or decreased activity, a sensation of stomach turning, nausea, and vomiting. There are minor changes in blood pressure, and the pupils become constricted (smaller). Drugs that alter perception include those above as well as marijuana, phencyclidine (PCP), and lysergic acid diethylamide (LSD). In general, most drugs of abuse can cause hallucinations under some circumstances. The drugs that more specifically affect perception (hallucinogens) produce a combination of depersonalization, altered time perception, body-image distortion, perceptual distortions (usually visual), and sometimes feelings of insight. Physiological effects such as changes in heart rate and blood pressure may also occur.

HARMFUL EFFECTS

This section reviews the harmful effects of alcohol and drugs. Alcohol and drugs contribute not only to the ill health of the individual, but directly to reckless behaviors that result in injury. For example, the impact of alcohol and drug abuse on the rate of motor vehicle accidents is well-known, but individuals under the influence of alcohol or drugs also engage in other dangerous behaviors at a high rate. They are more likely than others to harm themselves accidentally, as in falls or intentionally, as in suicide. They are also more likely to harm others, as when they engage in violent activities and/or in criminal behaviors.

Accidents. Alcohol is a significant factor in accident-related deaths. The main causes are motor-vehicle accidents, falls, drownings, and fires and burns. Approximately 50 percent of motor vehicle fatalities (driver, pedestrian, or cyclist) in the United States are alcohol-related, with the incidence having decreased slightly in the 1990s and early years of the twenty-first century. These alcohol-related accidents are more common at nights and on weekends. Falls are the most frequent cause of nonfatal accidents and the second most frequent cause of fatal accidents. Various studies indicate that alcohol is a factor in 17 to 53 percent of fatal falls and 21 to 77 percent of nonfatal falls (Hingson & Howland, 1987; Kool et al., 2008). Fatal falls occur at the highest rate among young males (Ramstedt, 2008). The higher the blood alcohol content (BAC), the higher is the risk for falls. The third leading cause of accidental death in the United States is drowning. About half (47–65%) of adult deaths by drowning are alcohol-related (U.S. Department of Health and Human Services, 2000). Fires and burns are the fourth leading cause of accidental death in the United States. Studies on burn victims show that alcohol intoxication is common. Cigarette smoking while drinking is a common cause of fires and burn injuries, with estimates of the rate of intoxication ranging from 37 to 64 percent. Users of other drugs of abuse (e.g., cocaine and opioids) also have higher rates of accidents than the non-drug-abusing population. The combination of cocaine and alcohol has been reported to be commonly associated with motor-vehicle deaths. Between 1984 and 1987 in New York City, 18 percent of motor-vehicle deaths showed evidence of cocaine use at autopsy. Cigarette smokers have higher rates of accidents than do nonsmokers. In an Australian study of fatally injured drivers, those drivers who tested positive for any psychoactive substance were significantly more likely than drug-free drivers to have been the individual responsible for the accident (Drummer et al., 2004). Drugs that alter perception, such as PCP, are

also associated with accidents mostly related to an impaired sense of judgment.

Crime. Associations between criminal activity and alcohol use have been established; however, a clear causal relationship between alcohol use and crime has not been established as of 2008. The strongest association between crime and alcohol use occurs in young males. Other forms of drug abuse (e.g., heroin and cocaine) have much higher associations with criminality. For example, the majority of persons enrolled in methadone programs have extensive criminal careers. Those involved in drug dealing are at a high risk of being either a perpetrator or a victim of homicide.

Family Violence. Several studies show an association between alcohol use/abuse and spousal abuse; however, the nature of this interaction was not well understood as of 2008. Intoxication is associated with negative behaviors among episodic drinkers, which are less common among steady drinkers, suggesting that drinking may be a short-term solution to problems for regular drinkers. Clearly, alcohol use is associated with physical violence in some families, and there also appears to be a link between alcohol and child abuse. Female caregivers with a diagnosis of alcohol abuse, alcohol dependence, recurrent depression, or antisocial personality are more likely to report physical abuse of their children than those without these diagnoses (Bland & Orn, 1986).

Suicide. Alcohol dependence is a risk factor for suicide; the lifetime risk of an alcohol-dependent individual committing suicide ranges from 2 to 18 percent. From 20 to 36 percent of suicide victims have a history of alcohol abuse or had been drinking prior to death. Alcohol use is linked more often to impulsive than to premeditated suicides and to the use of firearms rather than to other modes of killing. Death from overdose of illicit drugs is common; most of these are thought to be accidental but some are intentional.

Trauma or Severe Injuries. A history of trauma has been found to be a marker for (sign of) alcohol abuse. Emergency room trauma victims have high rates of intoxication. Furthermore, heavy alcohol use both interferes with recovery from serious injuries and increases rates of mortality for a given injury. Users of illicit drugs have a higher age-adjusted rate of mortality than do non-users. Many of these deaths result from trauma.

Effects in Pregnancy. Alcohol is firmly established as a teratogen (an agent that produces defects in the developing fetus) and is considered the most common known cause of mental retardation. Fetal alcohol syndrome (FAS) defects range from specific structural bodily changes to growth retardation and subtle cognitive-behavioral abnormalities. The diagnostic criteria for fetal alcohol syndrome include: prenatal (before birth) and postnatal (after birth) growth retardation; characteristic craniofacial defects; central nervous system (CNS) dysfunction; and organ system malformations. When only some of these criteria are met, the diagnosis is termed fetal alcohol effects (U.S. Department of Health and Human Services, 2000). The abnormalities in physical appearance seem to decrease with age, whereas the cognitive deficiencies tend to persist. There is no clear dose-response relationship between alcohol use and abnormalities. The safe amount of drinking during pregnancy (if it exists at all) is unknown. The peak level of blood (or brain) alcohol attained and the timing in relation to gestation (and particular organ development) are probably more important than the total amount of alcohol consumed during pregnancy. Genetic and maternal variables also seem to be important. Native American and African American children seem to be at high risk. While the public is generally aware of the relationship between alcohol consumption and fetal abnormality, surveys reveal that there is a need for greater public education in this area.

Use of other substances of abuse can also result in negative pregnancy outcomes. Smoking is associated with low birth weight. Cocaine use in pregnancy has been associated with complications (e.g., placental separation and in utero bleeding), and it appears to be associated with congenital abnormalities. Heroin use in pregnancy is associated with premature delivery and low birth weight; often there is a withdrawal syndrome in the baby at birth. Methadone (a long-acting opioid) usually reduces rates of prematurity and low birth weight but still causes as much or more opioid withdrawal in the newborn.

Cancer. Epidemiologic evidence exists for an increased risk of certain types of cancer in association

with alcohol consumption. These include cancer of the esophagus, oropharynx (mouth and throat), and liver. Other cancers possibly associated with alcohol consumption include cancer of the breast, stomach, prostate, and colon (Geokas, 1984). Alcohol plays a synergistic (multiplicative) role with smoking tobacco in the development of cancer, particularly with respect to the head, neck, and esophagus. There are several possible mechanisms through which alcohol enhances the onset of cancer. Alcohol appears to modify the immune response to cancers, facilitate delivery of carcinogens (substances which enhance cancer onset), and impair protective responses. Overall, alcohol is considered to act as a co-carcinogen; for example, it increases the likelihood of certain smoking-induced cancers.

Smoking is, of course, well established as a cause of lung as well as other cancers. Smoking is responsible for 85 percent of lung cancers and has been associated with cancers of the mouth, pharynx, larynx, esophagus, stomach, pancreas, uterine cervix, kidney, ureter, and bladder (Bartecchi et al., 1994). Chewing tobacco (smokeless tobacco) is associated with mouth cancer. The chewing of betel nuts with lime is common in Asia and results in the absorption of arecoline (a mild stimulant). This practice also causes cancer of the mouth. It has been suggested that marijuana smoking also causes lung cancer, since high tar levels are present in the smoked products.

ALCOHOL USE AND ABUSE AMONG ADOLESCENTS

Alcohol use among adolescents is a serious worldwide problem. Surveys indicate that up to 54 percent of eighth graders, and up to 84 percent of twelfth graders report having consumed alcohol (O'Malley et al., 1998). There is little doubt that parents' attitudes and habits concerning drinking are important influences on adolescent drinking (Ary et al., 1993). However, there is also evidence that adolescents who abuse alcohol often have coexisting psychopathology such as conduct disorder and bouts of depression and anxiety (Clark & Bukstein, 1998).

Another significant reason for concern about alcohol ingestion by adolescents is the close association of alcohol abuse with the use of other drugs. There is considerable evidence that alcohol use tends to precede the use of illicit drugs, and some researchers argue that, based on long-term studies, alcohol serves as a *gateway* to the use of illicit substances. Alcohol users were found to have a significantly higher prevalence of cigarette smoking, marijuana use, and cocaine use than non-users of alcohol, as early as the eighth grade. This difference persists through grade 12 and thereafter (Kandel & Yamaguchi, 1993). In one twin study, early use of alcohol by male adolescents (before age 17) was positively correlated with adult alcohol use and dependence and to the use of other drugs of abuse (Grant et al., 2006).

EFFECTS OF ALCOHOL AND OTHER DRUGS ON BODILY SYSTEMS

The toxic effects of alcohol on organ systems are pervasive, largely because alcohol mixes easily with water, and is thus distributed widely throughout the body. While alcohol is itself toxic, its effects are also mediated by acetaldehyde, a toxic metabolite. Tobacco also has pervasive toxic effects; when inhaled as cigarette smoke, its components escape metabolism by the liver and are introduced directly and rapidly into the bloodstream. Also like alcohol, the toxic effects of tobacco are due to more than one substance, chief among them nicotine, which is responsible for the cardiotoxic effects of tobacco, and tar, which has its greatest noxious effects on the lungs and mucus membranes. The toxic effects of other drugs of abuse on organ systems are more limited but still not insignificant.

Neurologic Effects. Acute alcohol consumption causes impairment as described above. Alcohol potentiates the action of many drugs that produce acute effects on the brain. High blood-alcohol levels can result in blackouts. This condition is the acute loss of memory associated with intoxication, although the person usually behaves in apparently normal fashion during this period. Blackouts are also seen with the ingestion of other CNS depressants, such as barbiturates and benzodiazepines.

The main adverse neural consequences of chronic alcohol consumption are the following: brain damage (manifested by dementia and alcohol amnestic syndrome); complications of the withdrawal syndrome (seizures, hallucinations); and peripheral neuropathy. Chronic alcohol consumption results

in tolerance, followed by an increased long-term consumption that likely leads to tissue damage. Physical dependence may also develop, manifested by a withdrawal syndrome on sudden cessation of drinking. The brain damage, when severe, is usually classified as one of two main disorders. The first is a type of global (general) dementia. It is estimated that 20 percent of those individuals admitted to state mental hospitals suffer from alcohol-induced dementia (Freund & Ballinger, 1988). The second is an alcohol-induced amnestic (memory-loss) syndrome, more commonly known as Wernicke-Korsakoff syndrome. This is related to thiamine (Vitamin B_1) deficiency. The *Wernicke* component refers to the acute neurologic signs, which consist of ocular (eye) problems such as a sixth cranial nerve palsy (disturbed lateral gaze), and ataxia (gross incoordination of muscle movements); the *Korsakoff* component refers to the memory impairment, which tends to be selective for short-term memory and is usually not amenable to treatment once it has become manifest.

Milder forms of these disorders are also detectable with neuropsychologic testing or brain imaging techniques (computed tomography [CT scans]; magnetic resonance imaging [MRI]). Studies of detoxified alcoholics (without other evidence of organic brain damage) reveal that 50 to 70 percent have impairments in neuropsychologic assessment (Eckardt & Martin, 1986). In most of these cases there is reversibility with abstinence from alcohol. Severe liver disease (e.g., acute hepatitis, advanced cirrhosis) may also contribute to this neurologic impairment. CT scans reveal that many alcoholics have cerebral atrophy, which consists of decreased brain weight, an increase in spaces (sulci) between various regions of the brain, and an increase in size of ventricles (spaces filled with cerebrospinal fluid). In a minority of cases, these structural changes are reversible with abstinence. Seizures are associated with heavy alcohol consumption and usually occur in association with alcohol withdrawal. Abstinence from alcohol is usually the only treatment needed for this type of seizure. The hallucinations that are mostly associated with alcohol withdrawal are usually treated with drugs: benzodiazepines and antipsychotics. *Peripheral neuropathy* is damage to peripheral nerves and is associated with chronic alcoholism. Direct toxic effects of alcohol and concurrent nutritional deficiencies cause this damage. The neuropathy results in changes in sensation and occasionally motor function, usually in the legs. Sometimes this condition can occur acutely with intoxication. For example, the abnormal posture in association with a drunken stupor can result in radial nerve (so-called Saturday night) palsy (paralysis of a body part that may be accompanied by loss of feeling and uncontrolled body movements). Alcoholics are also at increased risk of subdural hematomas (blood clots due to ruptured intracranial veins secondary to trauma) and of stroke. The neurologic complications associated with the acute use of other drugs of abuse (e.g., cocaine) include seizures (convulsions) and strokes.

Other drugs can also produce neurologic symptoms. High doses of some opioids, such as propoxyphene (Darvon) or meperidine (Demerol) cause seizures. Substances that can cause delirium (reversible disorientation and agitation) include cannabis (marijuana), phencyclidine (PCP), lysergic acid diethylamide (LSD), and atropine. Sudden cessation of use of CNS depressants (benzodiazepines, barbiturates, and alcohol) can result in seizures and hallucinations. Chronic use of other substances of abuse can also result in neurologic complications. Tobacco use is associated with increased rates of stroke (but it appears to be associated with lower rates of Parkinson's disease, a progressive disorder affecting control of movement). Solvent abuse (via inhalation) can cause damage to the cerebellum (the part of the brain controlling movement) and to peripheral nerves. A form of *synthetic heroin* (MPTP, 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine), an analog of meperidine (Demerol), has been demonstrated to cause a severe form of Parkinson's disease.

Psychiatric Effects. Alcohol-related diagnoses are common among psychiatric patients. For example, one study (Moore et al., 1989) showed that 30 percent of those admitted to a psychiatric unit had a concurrent alcohol-related diagnosis. Alcohol alone may produce symptoms and signs that mimic psychiatric disorders. Examples include depression, anxiety disorder, psychosis, and antisocial personality disorder. Alternatively, an alcohol-related disorder may coexist with one of these or may aggravate the psychiatric disorder. Alcohol as a CNS depressant tends to cause low mood states (hypophoria) with chronic use. It may cause or worsen clinical depression. If alcohol is the primary cause

of a depressed mood state, then abstinence from alcohol, as the sole treatment, rapidly improves the disorder. Hallucinations may occur during alcohol withdrawal, mimicking a psychotic disorder. Similarly, the anxiety associated with alcohol withdrawal may mimic an anxiety disorder. Anxiety and hallucinations may also be seen during withdrawal from sedative-hypnotics. Aggressive, illegal or irresponsible behavior associated with alcoholism may lead to an erroneous diagnosis of antisocial personality disorder.

When alcohol is used for self-medication in some psychiatric conditions, such as anxiety disorders, it tends only to be of short-term help and leads to more long-term problems. Other drugs of abuse, such as the stimulants cocaine and amphetamine, also produce anxiety and occasionally may produce a psychotic state during acute intoxication. This usually disappears rapidly as the drug effects wear off. Withdrawal following chronic use of stimulants may be associated with depression, excessive fatigue, and somnolence (a *crash*). Tobacco smoking also appears to be associated with depression. (Individuals with a history of depression are more likely to smoke and may develop depression when they try to stop.) Although the nature of the relationship is unclear, patients with psychiatric diagnoses (e.g., schizophrenia) have higher rates of smoking than the general population. Hallucinogens (such as LSD and PCP) commonly cause an acute psychotic disorder that typically disappears as drug effects wear off; however, in some cases there may be longer lasting effects. Antisocial personality disorder is a common pre-existing diagnosis in those who abuse alcohol and drugs.

Endocrine and Reproductive Effects. Alcohol produces both acute and chronic effects on virtually all endocrine organs (hormone-producing glands). Acutely, alcohol raises plasma catecholamines, which are chemicals released from nerve endings that are responsible for certain emotional reactions: the so-called fear, flight, and fight. Epinephrine (adrenaline) is released from the inside (medulla) of the adrenal gland and norepinephrine (noradrenaline) from sympathetic neurons (nerve cells) and the adrenal glands. Alcohol also causes release of cortisol from the outside (cortex) of the adrenal gland both acutely and chronically. Cortisol is a hormone (chemical messenger) responsible for multiple effects on the body, including changes in the immune response, glucose regulation, fat breakdown, blood pressure, and mood. Alcohol-induced cortisol excess can mimic Cushing's disease (a condition associated with excess cortisol production, often caused by a tumor on the adrenals) and is known as pseudo-Cushing's disease. Alcohol affects the hypothalamus (an area of the brain), where it modifies chemical-releasing factors, which in turn control release of hormones from the pituitary (a gland in the brain linked to the hypothalamus by a special blood supply), which in turn affect endocrine organs throughout the body. Acutely, alcohol also inhibits the release of antidiuretic hormone (ADH) from the posterior pituitary, which results in increased urine production. The best documented chronic endocrine effect of alcohol is male hypogonadism, a condition resulting from low sex-hormone function. Signs of the condition are small testes and decreased body hair. Symptoms include loss of libido (sex drive) and impotence. Hypogonadism can result from alcohol lowering testosterone levels both by direct effects on the testes and indirectly via the hypothalamus.

Alcoholic liver disease may also produce feminization in men, as a result of impaired metabolism (breakdown) of female sex hormones such as estrogen. Signs of such feminization in men include gynecomastia (enlarged breasts) and female fat distribution. In women who drink alcohol excessively, there is a high prevalence of gynecologic disorders (missed periods and problems in functioning of ovaries) and a possibly earlier onset of menopause than in nondrinkers. In women alcohol is metabolized at different rates according to the particular phase of the menstrual cycle. Other hormonal effects have been described in association with acute alcohol ingestion, including the impaired release of growth hormone and increased release of prolactin, a hormone involved in milk production. Thyroid function, which controls the body's rate of metabolism, can be indirectly affected as a result of alcoholic liver disease. This effect occurs from impaired conversion of T4 (a form of thyroid hormone) to T3 (a more active form of thyroid hormone). Furthermore, in alcoholism, there are abnormalities in the proteins to which thyroid hormone binds, making thyroid function tests difficult

to interpret. Overall thyroid function is usually normal despite mild abnormalities in the tests.

Other drugs, particularly the opioids, also have multiple effects on the endocrine system. Opioids produce a degree of hypogonadism as a result of lowered testosterone in males and disturbed menstrual function in females. This effect results from opioid inhibition of gonadotropin releasing hormone (GRH) in the hypothalamus, which in turn inhibits release of lutenizing hormone (LH) and follicle stimulating hormone (FSH) from the pituitary. Opioids also inhibit corticotropin releasing factor (CRF), which results in decreased adrenocorticotrophic hormone (ACTH) and decreased cortisol release. Nicotine causes release of epinephrine and norepinephrine, which in turn increase blood pressure and heart rate. Nicotine also enhances the release of ADH from the pituitary, which decreases urine output (i.e., it counteracts alcohol's effects).

Cardiovascular Effects. Alcohol has direct effects on both cardiac muscle and cardiac electrophysiology (electrical functioning). These effects are also dependent on the prior history of alcohol use (i.e., whether there have been underlying cardiac changes due to chronic use) and whether there is any evidence of underlying heart disease. Acutely, alcohol is a myocardial depressant (decreases heart muscle function), and chronically, it may cause a degeneration of cardiac muscle (known as cardiomyopathy), which can lead to heart failure (a condition in which excess body fluids and inadequate pumping function of the heart are present). Abstinence from alcohol leads to improvement in function in some cases. Both acute alcohol intoxication and acute withdrawal can lead to cardiac arrhythmias (abnormal heart rhythms). The most frequent association is with atrial fibrillation (frequent uneven and uncoordinated contraction of the atria, the blood collection chambers of the heart). This condition is usually not life threatening and mostly disappears without specific treatment. Multiple epidemiologic studies have established a relationship between alcohol and high blood pressure (hypertension). Between 5 and 24 percent of hypertension is considered to be alcohol related (Klatsky, 1987). The relationship seems to hold most strongly for white males over the age of 55, consuming at least 3 standard drinks per day on a chronic basis. Many cases resolve with abstinence. Acute alcohol withdrawal is often associated with hypertension, but this condition usually lasts for only a few days.

High levels of alcohol consumption are associated with increased rates of coronary heart disease (disease of the blood vessels that supply heart muscle), while low levels of consumption (in comparison to complete abstinence) may be associated with a mild protective effect. Evidence for an inverse relationship between moderate alcohol consumption and coronary heart disease is derived from epidemiological and clinical case-control and cohort studies. Early investigators, impressed by the relatively low incidence of coronary heart disease in France despite an intake of saturated fats at least three times that of the United States (the so-called French paradox), focused their studies on the potential cardioprotective properties of red wine (Klatsky et al., 2003). Other studies, however, indicate that all alcoholic beverages—wine, beer, and liquor—when consumed in moderation, are associated with a lower coronary artery disease risk (Rimm et al., 1996). In dose-range studies, the equivalent of two alcoholic drinks per day was associated with a decreased incidence of coronary heart disease compared with no drinks, whereas higher doses result in an increased risk of infarction as well as the well-known problems produced by alcohol excess. Scientists describe this relationship between alcohol intake and coronary heart disease-when shown graphically—as a J-shaped or U-shaped curve, with the greatest benefit accruing at moderate doses, which correlate with the lowest point on the curve. Individuals may find themselves caught in a dilemma between the oft-preached dangers of drinking and these acclaimed benefits. Because most American households already are exposed to alcohol (Thun et al., 1997), advice as to the benefits of moderation may be offered without reserve. However, low levels of consumption are not recommended specifically as a preventive measure against coronary heart disease. In the case of abstainers, the risks of initiating alcohol consumption may outweigh its potential benefits. This reservation is especially applicable in families that include adolescents.

Chronic tobacco use is the most important of the preventable causes of coronary heart disease, and cigarette smoking is a much greater risk factor than

is alcoholism. It should be noted, however, that in some studies, 80 to 90 percent of alcoholics are also cigarette smokers, though this high a prevalence of smoking is not universal. Acutely, nicotine results in constriction (narrowing) of blood vessels and an increase in heart rate. The coronary arteries supply the heart muscle. Long-term tobacco use results in an increase in atherosclerosis (build up of fat and other products inside the walls of blood vessels) in most of the arteries throughout the body and increases coagulation (clotting). This has important adverse effects on the coronary arteries (causing angina [chest pain] and infarction [heart attack]); the aorta (causing aneurysms, a ballooning effect on the arterial wall, which can be fatal); the carotid arteries (which can cause strokes); the femoral arteries (causing intermittent claudication, or pain on walking); and the renal arteries (causing kidney failure and some hypertension).

The acute use of cocaine (a stimulant) results in increases in heart rate and blood pressure and causes narrowing of peripheral and coronary arteries. Repeated use of cocaine has been associated with abnormal heart beats, myocardial infarction (heart attack), and possibly myocardial fibrosis (an increase of scar tissue within the heart). Acute use of opioids has minor effects on blood pressure. There are no important chronic adverse effects of opioids on the cardiovascular system. Marijuana acutely causes increases in heart rate and blood flow.

Respiratory System Effects. Acutely, alcohol does not usually interfere with lung function; however, a decrease in cough reflexes and a predisposition to reflux (regurgitate) stomach fluids into the lungs can result in the impairment of bacterial clearance in the respiratory tract after intoxication. Chronic alcohol consumption is associated with several pulmonary infectious diseases; these include pneumonia, lung abscess, and tuberculosis. Aspiration pneumonia occurs in association with high levels of alcohol intoxication; it is thought to be caused by the inhalation of bacteria caused by the impairment of the usual reflexes, such as coughing. For some persons with asthma, alcoholic beverages can induce bronchospasm (airway narrowing). This condition is thought to be related to non-alcoholic components in the beverage. Acute alcohol consumption also has a direct depressant effect on the respiratory center located in the brainstem. Accordingly, an overdose (intentional or unintentional) can result in death from respiratory failure (decreased ability to breathe). Alcohol also contributes to respiratory depression when taken with other central nervous system depressants such as barbiturates and benzodiazepines (minor tranquillizers). Acute alcohol intake worsens sleep apnea, a condition in which breathing ceases for periods of time during sleep. Pancreatitis and alcoholic cirrhosis are associated with pulmonary effusions (build-up of fluid around the lung).

Cigarette smoking causes emphysema, chronic bronchitis, and lung cancer. The smoking of marijuana on a frequent long-term basis may also increase the likelihood of these disorders, though this correlation has not been definitively proven. Acutely, the intravenous injection of opiate drugs may cause pulmonary edema (accumulation of fluid in the lungs), which can be life-threatening. Chronic use of intravenous drugs may cause pulmonary fibrosis (scar tissue in the lung). This effect is probably related to impurities, such as talc, associated with the cutting of the drug (diluting the dose with fillers) prior to its sale and eventual injection.

Effects on the Gastrointestinal Tract and Pancreas. Acutely, alcohol alters motor function of the esophagus. Chronic use of alcohol increases gastroesophageal reflux. Alcohol alone does not appear to cause peptic ulcers (as smoking cigarettes does), but alcohol interferes with healing. Alcohol disrupts the mucosal barrier in the stomach and causes gastritis (inflammation of the stomach), which can lead to hemorrhage, especially when combined with aspirin. Alcohol also interferes with the cellular junctions within the small intestine, which can result in the disturbance of fluid and nutrient absorption, producing diarrhea and malabsorption. Any resulting nutritional deficiencies can further aggravate this process.

Heavy drinking interferes significantly with pancreatic structure and function. Alcohol abuse and gallstone disease are the major causes of pancreatitis, and alcoholism alone is responsible for most cases of chronic pancreatitis. Alcohol changes cellular membranes, disrupting transport mechanisms and the movement of vital ions and nutrients essential for normal cellular function. Acetaldehyde,

a breakdown product of alcohol (and also present in cigarette smoke), is toxic to cells and has been proposed as a causative agent in the development of this disorder (Geokas, 1984). Acute pancreatitis is life threatening; patients have abdominal pain, nausea, and vomiting. Increased levels of pancreatic enzymes, such as amylase and lipase, accompany this disorder. Treatment is usually by conservative measures, such as replacement of fluids and pain relief. Chronic pancreatitis may occur without symptoms, or it can become evident due to the occurrence of chronic abdominal pain and evidence of malabsorption (weight loss, fatty stools, and nutritional deficiencies) or, uncommonly, with the appearance of diabetes mellitus resulting from the destruction of the endocrine as well as the exocrine function of the pancreas.

Liver Effects. Alcoholic liver disease is a major cause of morbidity and mortality in the United States; in 2004 chronic liver disease and cirrhosis of the liver was the twelfth leading cause of death. Alcohol causes three progressive pathological (abnormal) changes in the liver: fatty liver, alcoholic hepatitis, and cirrhosis. These changes are useful in a prognostic sense but can only be diagnosed with a liver biopsy (in which a needle is inserted in the liver to obtain a small amount of tissue for study), which is not always feasible or practical. More than one pathological condition may exist at any one time in a given patient. Fatty liver, the most benign of the three conditions, is usually completely reversible with abstinence from alcohol; it occurs at a lower threshold of drinking than do alcoholic hepatitis and cirrhosis. Alcoholic hepatitis ranges in severity from no symptoms at all to severe liver failure with a fatal outcome; it can be followed by complete recovery, chronic hepatitis, or cirrhosis. Treatment is primarily supportive.

Similarly, the symptoms and signs of cirrhosis range from none at all to coma and death. Cirrhosis consists of irreversible changes in liver structure resulting from an increase in scar tissue. A consequence of this condition is an abnormal flow of blood through the liver (shunts), which can result in bleeding and the presentation of toxic substances (e.g., ammonia) to the brain. This, in turn, may result in effects ranging from impaired thinking to coma and death. Abstinence from alcohol can prevent progression of cirrhosis and reduces mortality and morbidity (illness) from this condition. Medications may also help to reduce mortality from alcoholic liver disease. One medication, propothiouracil (an antithyroid drug), is thought to work by reducing oxygen requirements, though its efficacy has yet to be proved. The efficacy of another medication, prednisone (a steroid), which reduces inflammation, appears to be limited. One promising new approach under investigation involves agents that work against tumor necrosis factor, a pro-inflammatory cytokine (chemical messenger) implicated in the pathophysiology of alcoholic liver disease. Women appear to be at higher risk for liver damage than are men.

Opioid use alone has not been associated with liver disease, but some opioids such as morphine can cause spasm of the bile duct, which results in acute abdominal pain. Tobacco use is associated with a more rapid metabolism (breakdown) of certain drugs in the liver, which means that sometimes higher or more frequent dosing of medications is required for smokers. This effect is thought to relate to the tars in tobacco rather than to the nicotine. High doses of cocaine have been associated with acute liver failure.

Acute and chronic viral hepatitis (types B, C, and D) is common in users of intravenous drugs. It is not the drug itself that causes hepatitis (inflammation of the liver) but rather the introduction of the viruses associated with the sharing of needles or other drug paraphernalia. Viruses and bacteria introduced by injecting drugs cause other problems, such as HIV infection and AIDS, endocarditis (infection of heart valves), cellulitis (skin infection), and abscesses.

Immune System Effects. Alcohol affects the immune system both directly and indirectly. It is often difficult to discern the direct effects of alcohol from concurrent conditions, such as malnutrition and liver disease. Alcohol affects host defense factors in a general way; it also seems to predispose those who drink heavily to specific types of infection. With respect to host factors, alcohol alone can reduce both the number and function of white blood cells (both polymorphonuclear leucocytes and lymphocytes). This effect predisposes toward infection while it interferes with the ability to counteract infection. Mechanical factors are also important. For example, alcohol intoxication resulting in

a depressed level of consciousness (and depressed cough reflex) predispose toward aspiration pneumonia. Specific infections for which alcoholics are at higher risk, compared to the population at large, include pneumococcal pneumonia (the most common form of pneumonia), other lung infections (e.g., Hemophilus influenzae, Klebsiella), abscesses (anaerobic infections), and pulmonary tuberculosis. Alcoholics with liver disease are at increased risk of spontaneous bacterial peritonitis (inflammation of the lining of the abdominal cavity). Other infections possibly associated with alcoholism include bacterial endocarditis (infection of the heart valves), bacterial meningitis (infection of the covering of the brain), pancreatitic abscess, and diphtheria (an infectious disease). HIV-infected drug abusers are at increased risk of tuberculosis as well as a multitude of other infections. As mentioned above, injecting drug users are also susceptible to a variety of infections associated with the use of non-sterile equipment. Changes in immune function have been reported to occur in users of other drugs of abuse, including heroin, cocaine, and marijuana. The precise relationship of the immune function change to the drug of abuse is not understood as of the early twenty-first century. Lifestyle factors such as poor nutrition are also likely to contribute to this connection.

Nutritional Effects. In heavy alcohol consumers, malnutrition is common and results from several conditions. Alcohol abusers often have poor dietary habits, resulting from the irritating effects of alcohol on the stomach lining. Alcohol also provides a significant number of calories per serving (7.1 kcal/gm), depressing appetite further. In some cases, alcoholics will subsist on alcohol alone without eating food over extended periods of time. In women, heavy alcohol consumption is associated with lower than usual body weight to a degree similar to that also associated with tobacco smoking; there is less weight-lowering effect in men. Specific nutritional disorders associated with alcoholism include anemia (due to iron or folate deficiency); thiamine (Vitamin B_1) deficiency, causing beriberi or Wernicke's encephalopathy or neuropathy; malabsorption; and defective immune and hormonal responses. Alcohol also interferes with the absorption of vitamins (such as pyridoxine and Vitamin A), minerals (such as zinc), and other nutrients (such as glucose and amino acids) (Mezey, 1985).

Abuse of other drugs also can lead to malnutrition, though specific syndromes have not been identified as of the early twenty-first century. Tobacco use is associated with depressed appetite as well depletion of Vitamins A and C. Amphetamines and cocaine are stimulants and have the effect of suppressing appetite. Drug-seeking behavior may also result in a general indifference toward food.

Metabolic Effects. Alcohol is metabolized (broken down) in the liver to acetaldehyde and hydrogen and then to carbon dioxide and water. Acetaldehyde is toxic to many different cellular functions. Alcohol affects carbohydrate, lipid (fat), and protein metabolism. Alcohol can cause low blood glucose (hypoglycemia) due to inhibition of glycogen (liver stores of carbohydrate) metabolism. Alcohol also raises blood sugar and acids (alcoholic ketacidosis). By interfering with the elimination of uric acid, alcohol may precipitate acute attacks of gout. Increased urinary excretion of magnesium can result in muscle weakness. Alcohol causes disturbances in blood lipids, mostly increases in triglycerides and high density lipoprotein (HDL) cholesterol.

Acute alcohol consumption can decrease, whereas chronic consumption can increase, the metabolism of certain drugs. Tobacco smoking also increases the metabolism of some drugs, such as theophylline and caffeine. This response results from the increased activity of various liver enzymes as discussed above.

Hematologic (Blood) Effects. The effects of alcohol on the hematologic system can either be direct, or it can be indirect (as a result of liver disease or nutritional deficiencies). Uncommonly, acute consumption of a very large dose of alcohol in a short time has direct effects on the bone marrow, resulting in decreased production of red cells, white cells, and platelets. Anemia is a common problem in alcoholics and may be due to a variety of factors. The most frequent effect seen in alcoholics following chronic consumption is an increase in the size of the red blood cells (macrocytosis). This increase is mainly due to direct toxic effects on the red cell membrane but may also be due to a deficiency of folate, a vitamin found in green vegetables. Folate deficiency in alcoholics is caused mainly by impaired intake and absorption of folate.

Iron deficiency anemia is also seen because of impaired intake of iron and because of frequent bleeding (due to a variety of factors, such as coagulation defects, gastritis, and the impaired healing of peptic ulcer). Iron-overload syndromes are also diagnosed in alcoholics and are due to multiple causes. Chronic alcohol consumption can also lead to hemolytic (excess breakdown of red blood cells) anemia, which is mainly seen in association with liver disease. Platelet production and function can be suppressed by alcohol, resulting in prolonged bleeding times. Other drugs also exert hematologic effects. Experimental addiction to opioids results in a reversible anemia and a reversible increase in erythrocyte sedimentation rate (a nonspecific indicator of the presence of a disease process). Smoking allows carbon monoxide to enter the body and bind to hemoglobin (carboxyhemoglobinemia), which consequently causes an increase in red cell production (erythrocytosis). The hematocrit value (the proportion of blood attributable to red blood cells) and the plasma fibronogen (a clotting factor) rise and increase blood viscosity; platelets (sticky constituents of blood important in wound healing) aggregate more in smokers. These thickening factors, together with damage to the insides of blood vessels, increase the probability of both stroke and heart attack (myocardial infarction) in smokers. White cells are also at increased levels in smokers (leucocytosis).

Skeletal Muscle Effects. Chronic alcohol consumption can result in muscle cell necrosis (death). Two main patterns are seen: (1) An acute alcoholic myopathy (disturbance of muscle function) occurs in the setting of binge drinking, sometimes associated with stupor and immobilization. This condition results in severe muscle pain, swelling, elevated creatine kinase (a muscle enzyme), and myoglobinuria (muscle protein in the urine which can cause kidney failure). (2) This pattern consists of a more slowly evolving syndrome of proximal muscle (those closest to the trunk) weakness and atrophy (decreased size). Milder degrees of muscle injury are quite common and consist of elevated levels of the muscle enzyme creatine kinase. Cocaine use can also cause muscle damage (rhabdomyolysis), resulting in abnormalities of creatine kinase. Most drugs of abuse (especially depressants) may indirectly cause muscle damage as a result of prolonged abnormal posture, for example, sleeping in an intoxicated state on a hard surface.

Renal Effects. Alcohol abuse causes a variety of electrolyte and acid-base (blood chemistry) disorders, which include decreases in the levels of phosphate, magnesium, calcium, and potassium. These abnormalities relate to disorders within the functioning kidney tubules (involved in secretion and reabsorption of minerals). The abnormalities usually disappear with abstinence from alcohol.

Heroin use has been associated with a form of kidney failure known as heroin nephropathy. Its precise relationship to heroin use is unclear and may be due, instead, to adulterants used to dilute the drug or to viral diseases such as hepatitis C or HIV that are spread through intravenous drug use. Secondary effects on the kidneys from drug and alcohol abuse also occur (for example, from the effects of trauma or muscle damage as described above).

See also **Crime and Alcohol; Crime and Drugs; Inhalants; Intimate Partner Violence and Alcohol/Substance Use; Social Costs of Alcohol and Drug Abuse; Substance Abuse and AIDS; Tobacco: Medical Complications.**

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CARDIOVASCULAR SYSTEM (ALCOHOL AND COCAINE)

Alcohol remains the most commonly used drug of abuse in the United States. Between 5 and 10 percent of the male population may be considered alcohol abusers with upwards of 21 percent of hospital admissions having an alcohol-related diagnosis. At least 500,000 deaths per year can be attributed to alcohol abuse. Excessive alcohol consumption increases mortality but also causes preventable illness. Alcohol abuse increases morbidity among hospitalized patients and plays a major role in admissions and mortality of patients in ICUs. Ethanol-related disorders consume as much as 20 percent of total health-care expenditures in the United States.

What constitutes excessive ingestion of alcohol has been determined. A standard serving (14 g of ethanol) of alcohol translates into 12 ounces (340 ml) of beer (5% alcohol v/v); 5 ounces (142 ml) of wine (12.5% alcohol v/v); and 1.5 fluid ounces (43 ml) of 80-proof spirits (40% alcohol v/v). *National Institute on Alcoholism and Alcohol Abuse Guidelines* recommends that men consume no more than 14 drinks per week and no more than four drinks per day. For women the amounts are lower, with no more than seven drinks per week and one to two drinks per day. These estimates are higher than those considered *moderate drinking* by many health providers, which recommend one and two drinks a day for women and men, respectively. Beneficial or adverse effects of drinking on the

body are related to the amount consumed. Many Americans routinely consume more than the recommended serving and number of drinks.

PROTECTIVE EFFECTS OF ETHANOL INGESTION

Light-to-moderate drinking has beneficial effects on cardiovascular health through increases in high-density lipoprotein cholesterol, attenuation of inflammatory responses, and/or changes in blood clot formation. One to two glasses of red wine per day reduces the risk of cardiovascular disease, particularly coronary artery disease, suggesting that drinking red wine overcomes risks for coronary artery disease posed by high serum cholesterol concentrations (referred to as the *French Paradox*). A positive association exists between moderate alcohol use and survival in heart attack patients wherein both heavy drinkers and abstainers have poorer prognoses. Risk of blockage reforming in coronary arteries is lowered after stent implantation in patients consuming moderate amounts of alcohol. Light and moderate alcohol consumption raises blood concentrations of high-density lipoprotein (HDL), the so-called good cholesterol. About one-half of the protection afforded by moderate ethanol consumption is ascribed to an increased HDL cholesterol concentration in the blood. However, this protection vanishes if ethanol consumption is high enough to induce severe liver disease. Light to moderate alcohol drinking elevates plasma apolipoproteins, the plasma proteins that transport cholesterol in the blood, which also seems to afford a certain degree of protection.

Ethanol protects against clot formation by inhibiting platelet activation and platelet thrombus formation by interfering with the precursor of protaglandins, arachidonic acid, mobilization and subsequent inhibition of thromboxane A2 synthesis. Thromboxane A2 promotes platelet aggregation and contributes to clot formation with corresponding narrowing of coronary arteries. Reducing thromboxane A2 following ethanol ingestion decreases clot formation thereby preventing reductions in coronary blood flow. Ethanol may maintain coronary vessel blood flow through dilatation of coronary arteries and other mechanisms that protect the heart from injury. Moderate alcohol ingestion improves post-heart attack functions and increases nitric oxide production (a potent vasodilator) by the coronary arteries. All of these mechanisms promote coronary blood flow, preventing reductions in oxygen delivery to jeopardized heart muscle at risk for ischemic injury. Active metabolites including polyphenolics, such as resveratrol within alcoholic beverages but primarily red wine, may prevent cardiovascular disease. Red wine enhances the dilation of blood vessels in patients with elevated cholesterol levels. Dealcoholized red wine, red wine, or resveratrol prevent cholesterol-induced reductions in coronary blood flow. Thus several mechanisms may account for the original description of the beneficial effects of moderate red wine drinking on cardiovascular function.

ACUTE DETRIMENTAL EFFECTS OF BINGE DRINKING ON THE DEVELOPMENT OF ARRHYTHMIAS

The *holiday heart syndrome* occurs as a result of alcohol-induced arrhythmias (abnormal heart rhythms), in otherwise healthy individuals. The chief arrhythmia is atrial fibrillation, which is described as rapid, irregular twitching of the atrial muscle. The syndrome was first described in heavy drinkers, who typically presented with symptoms of irregular heart rhythm on weekends or after holidays, but it may also occur after binge drinking in patients who usually drink little or no alcohol. The rhythm disorders usually convert to normal sinus rhythm within 24 hours of cessation of ethanol consumption. The association between alcoholic beverage ingestion and atrial fibrillation has been questioned when analysis is done using large (presumably, unbiased) populations of individuals.

Ethanol enhances sympathetic activation and increases norepinephrine release. Norepinephrine activates cardiac adrenergic receptors and initiates a cascade of events that result in increased heart rate and strength of contraction of the heart muscle. Higher doses initiate arrhythmias characteristic of holiday heart syndrome. Ethanol may also reduce parasympathetic activity and decrease heart rate variability, factors known to predispose the myocardium to arrhythmias. Although acute alcohol abuse most commonly causes atrial arrhythmias, it can also increase the risk of ventricular arrhythmias, a prime factor leading to sudden cardiac death in people who consume large quantities of alcohol. Ethanol-induced inhibition of cardiac sodium movement across cardiac muscle

membranes via specific channels provides one potential mechanism for triggering supraventricular and ventricular arrhythmias. Following cessation of alcohol consumption, both low blood potassium and magnesium increase the risk for development of arrhythmias secondary to altered plasma electrolyte imbalances. In addition to possible electrophysiological derangements, repeated doses of ethanol depress left ventricular ejection fraction at blood alcohol concentrations seen with moderate to severe alcohol intoxication.

ADVERSE CARDIOVASCULAR EFFECTS OF HEAVY DRINKING

Heavy drinking is detrimental to the heart, leading to increased mortality that appears independent of coronary arterial disease. Alcoholics generally present with greater left ventricular dysfunction but exhibit a lower incidence and less severe narrowing of coronary arteries than patients complaining of chest pain. Excessive ethanol consumption can result in a syndrome termed *alcoholic heart muscle disease* (AHMD). AHMD is rarely produced by short-term ethanol administration. In general, alcoholic patients consuming more than 90 grams of alcohol per day (approximately seven to eight standard drinks per day) for more than 5 years are at risk for the development of asymptomatic AHMD. Those alcoholics who continue to drink develop symptoms associated with defects in the ability of the heart to pump blood. With continued heavy drinking, AHMD progresses with the development of an alcoholic cardiomyopathy with the signs and symptoms of heart failure. Long-term heavy alcohol consumption is the leading cause of a non-ischemic, dilated cardiomyopathy, herein referred to as *alcoholic cardiomyopathy*. Patients with an alcoholic cardiomyopathy have a worse outcome than patients with an idiopathic dilated cardiomyopathy if drinking is not abated or severely arrested.

Alcohol-induced cardiac muscle injury produces an initial decline in cardiac pumping capacity. Following this initial decline, a variety of compensatory mechanisms are activated, including the adrenergic nervous system, the rennin-angiotensin system, and the cytokine response. Some of these compensatory changes have been detected in alcoholic patients. In the short term, these compensatory systems restore cardiovascular function to within a normal range so that the alcoholic patient remains asymptomatic. However, with time, the sustained activation of these systems can lead to secondary damage to the ventricle, activating and accelerating the subsequent decompensation of the heart's pumping function, resulting in the transition from asymptomatic to symptomatic heart failure.

Chronic heavy drinking (more than 90 grams per day for more than 5 years) is the initial insult that modifies myocardial function in humans, eventually producing derangements in myofibrillar architecture, including disarray of the contractile elements and cardiac function resulting in reduced cardiac output. The degree of dysfunction is dependent upon the duration of alcohol drinking and amount of ethanol consumed. Because of difficulties in obtaining serial measurements in humans, various rodent models have been used to mimic the pattern of human alcohol consumption. The thickness of the left ventricular wall does not diminish in hearts from rats with short-term exposure to a diet containing alcohol. However, prolonged alcohol exposure leads to decreases in myocardial protein followed by a decrease in left ventricle mass, ventricular wall thickness and posterior wall thickness. The structural abnormalities are followed by a decrease in cardiac output secondary to reduced stroke volume rather than changes in heart rate. With extended alcohol exposure, signs of progressive heart disease appear with evidence of further myocardial derangements associated with the evolution of the myocardium to a dilated cardiomyopathy. This was exemplified in rodents through alcohol-induced increases in end-diastolic diameter, end-systolic diameter, and left ventricular mass. In addition, the left ventricle pressure-volume relationship was shifted down and to the right, characteristic of a dilated ventricle cardiomyopathy. Hence a slow, progressive, left ventricular dilation and wall thinning continues until there are symptomatic signs of heart failure with systolic dysfunction observed with continued heavy drinking.

Ethanol decreases cardiac function via 1) changes in the myocardial handling of calcium ion fluxes that are necessary for proper contraction and relaxation of the heart, 2) the abundance of proteins (actin and myosin) that serve to physically contract the muscle, and 3) the covalent binding of reactive molecules to proteins. Ethanol depresses cardiac contractile

function by decreasing the rate and extent of pressure development and slowing the rate of relaxation in whole heart or depression of the development of tension in isolated cardiomyocytes.

Sex Differences in Response to Chronic Alcoholism. Men and women are adversely affected by heavy drinking. The acute response to binge drinking does not differ by sex. However, with long-term drinking sex-dependent differences appear. Women report lower lifetime cumulative levels of drinking than men. Females respond to chronic alcohol abuse in a fashion distinct from males. Initially women may be protected from detrimental effects of alcohol in that there is a lower degree of cardiac dysfunction and loss of the contractile proteins, actin and alpha myosin. As the duration of alcohol abuse increases females exhibit more severe declines in cardiac muscle contractility leading to severe reductions in ejection fraction in dilated cardiomyopathies.

ADVERSE EFFECTS OF COCAINE ON THE HEART

Cocaine is the second most commonly used illicit drug in the United States. In 2005, there were 448,481 cocaine-related visits to emergency departments in the United States with an over representation of 35 to 44 year olds. The frequency of cocaine-related medical emergencies has increased concomitant with the rise in drug use. Chest discomfort was reported in 40 percent of patients who presented to the emergency department after cocaine use; however, the cause of the chest pain remained obscure as of 2008. Cocaine use accounts for one-fourth of all non-fatal heart attacks in young patients.

The cardiovascular complications of cocaine abuse are adrenergic and include cocaine-associated acute coronary syndromes, myocardial ischemia and infarction, aortic dissection, and sudden cardiac death. Cocaine increases heart rate, elevates blood pressure, and enhances vasomotor tone, which are worsened by alcohol ingestion. Cocaine blocks the reuptake of norepinephrine and dopamine at the presynaptic adrenergic terminals, causing an accumulation of catecholamines at the postsynaptic receptor, thus acting as a powerful sympathomimetic agent. In addition, the ability of the vasculature to deliver oxygen is compromised by cocaine's ability to increase platelet aggregation and may produce a narrowing of coronary vessels following vasoconstriction of large epicardial and small coronary resistance vessels. Delayed or recurrent constriction of the coronary arteries may occur hours after the serum cocaine concentration has declined and appears to be caused by cocaine's major metabolites (breakdown products). The cocaine-induced surge in catecholamine concentrations elevates shear-stress forces, increasing the risk of a tear in vessel walls and aortic dissection. The net effect is that cocaine leads to enhanced myocardial demand by increasing heart rate, blood pressure, and contractility, and lowers oxygen delivery through vasoconstriction of coronary vessels.

Cocaine directly blocks the sodium channels in heart muscle cells and may produce or worsen cardiac arrhythmias. Cocaine increases the risk of ventricular fibrillation. It is speculated that the increase in left ventricular mass (associated with long-term cocaine use) and the development of fibrotic areas serve as the underlying anatomic substrate, increasing the propensity for ischemia and arrhythmias.

Cocaine abuse induces acute or chronic deterioration of left ventricular performance. Acute left ventricular systolic and diastolic dysfunction has been attributed to the effects of cocaine or its metabolites on the handling of calcium by heart muscle cells. In addition, intravenous administration of cocaine can lead to infective endocarditis with subsequent damage to heart valves and deterioration of heart function. The use of cocaine appears to be a greater independent risk factor than the use of other drugs for the development of endocarditis. One possible explanation is that the elevation of the heart rate and systemic arterial pressure that accompanies cocaine use may induce valvular and vascular injury predisposing cocaine users to bacterial invasion. Cocaine use may also increase the risk of infection by lowering an individual's immune response to bacteria. Cocaine addiction induces protracted decreases in innate immune mechanisms lowering the host's ability to combat microbial invasion. With intravenous use, the adulterants or non-cocaine processing ingredients that are often present in cocaine may cause endocarditis with the ensuing

cardiovascular complications associated with valvular heart disease.

The effects of ethanol on the mammalian heart are complex and are dependent upon both the amount and duration of alcohol consumption. Low or moderate ethanol consumption provides protection from cardiovascular disease. Excessive drinking is associated not only with increased mortality, but also with premature death and preventable ill health. Binge drinking increases the potential for arrhythmias that generally rectify themselves following abstinence from further drinking. Alcoholic patients consuming approximately seven to eight standard drinks per day for more than ten years are at risk to develop asymptomatic alcoholic heart muscle disease. Individuals who continue to drink may develop the signs and symptoms of overt heart failure. The point at which changes in normal physiological function culminate in intrinsic cell dysfunction is incompletely understood as of 2008.

The biggest public health challenge is to identify patients who are at risk but not yet symptomatic of alcohol-induced cardiac muscle disease and to develop strategies to prevent the transition to a symptomatic disease stage. Unfortunately, the general population is not routinely screened for asymptomatic alcoholic heart muscle disease. Pronounced left ventricular dilation, wall thinning, systolic dysfunction, and signs and symptoms of overt heart failure characterize symptomatic alcoholic heart muscle disease. Treatment involves complete abstinence or a severe reduction in ethanol consumption coupled with treatment of the heart failure.

Cocaine addiction gives rise to a separate set of problems and often culminates in cardiac arrhythmia. The combination of alcohol and cocaine may be even more dangerous than cocaine alone. In the presence of alcohol (ethanol), in humans, cocaine is metabolized to the compound cocaethylene. This chemical renders the combination of cocaine and alcohol more lethal than either alone.

See also **Alcohol: History of Drinking (International); Cocaine; Overdose, Drug (OD); Prevention, Education and.**

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COGNITION

Psychoactive drugs of abuse are used for their perceived mind-altering effects; however, the drug user may not be aware of additional cognitive effects produced by the drugs. A cognitive effect is an impact on mental functions such as the processes of learning, perceiving, imagining, remembering, feeling, thinking, reasoning, knowing, and judging.

Psychoactive drugs produce cognitive effects by causing chemical changes in the brain. These effects

are frequently short-lived and correspond to the duration and intensity of the chemical changes in the brain. However, cognitive effects can persist after the drug has been eliminated from the body, and some can be irreversible.

ALCOHOL

Ethanol (also called ethyl alcohol) is the consumable alcohol content in beer, wine, distilled spirits, or medicinal compounds; it acts by depressing or reducing cognitions. Initially, alcohol reduces inhibitions, which results in more spontaneity or impulsivity and a feeling of relaxation. As the amount of alcohol acting on the brain increases, the ability to perceive, remember, reason, and judge is progressively impaired. Executive functioning, including planning and working memory, may also become impaired, even with a moderate dose of alcohol. Further increases in the amount of alcohol can depress the brain and cognitions to the point of loss of consciousness. Because of the cognitive impairment the person may not perceive the impairment (e.g., "I'm not drunk") and may take undue risks (e.g., drunk driving and other indiscretions).

Alcoholic blackouts are impairments of the memory of events that occurred while conscious but under the influence of alcohol. Such blackouts are not limited to chronic alcoholics. Long-term use of alcohol can lead to subtle impairment of perceiving, responding, and remembering that may not be detectable without formal neuropsychological testing. As many as two-thirds of abstinent alcoholics in treatment have some impairment in learning, memory, problem solving, and perceptual motor skills. Overall intelligence and language skills are typically spared. There is considerable evidence that cognitive recovery begins about two weeks following detoxification and can continue for several years in alcoholics who remain abstinent. The aging brain is more susceptible to the effects of alcohol than is the brain of a younger alcohol abuser. Consequently, the probability of making a full recovery decreases with age. Alcohol dementia is the most severe form of alcohol-related cognitive impairment and includes profound amnesia. Moreover, deficits can persist throughout a person's life even if they stop drinking.

Paranoid states of unfounded suspicion or jealousy may manifest or be aggravated under the influence of alcohol. In alcoholic hallucinations, people can have vivid but unreal perceptions while conscious; these typically occur as a result of neurochemical changes in the brain when alcohol use is abruptly discontinued after periods of excessive drinking.

TRANQUILIZERS, SEDATIVES, AND HYPNOTICS

These drugs are often collectively referred to as *downers*. People taking them are at risk for the same cognitive impairments produced by the consumption of alcohol. The elderly are particularly at risk for confusion.

STIMULANTS

Stimulant drugs have effects that are the reverse of depressant drugs: They arouse the nervous system. These drugs include cocaine, amphetamines (speed), and caffeine. In low doses perception is heightened, attention is increased, and thought processes are accelerated, resulting in a feeling of greater alertness. Memory, however, can be affected resulting in impaired recall of material learned while under the influence of stimulants. Higher doses intensify the above effects and lead to restlessness and rapidity of thoughts, which reduce attention. Vulnerable people can become paranoid or even psychotic. Higher effective doses of stimulants can occur via intravenous administration or inhalation of cocaine, rapidly affecting the brain and resulting in an abrupt *rush* or *high*. These effects are typically short-lived but are so intensely pleasurable that individuals often repeat doses. Discontinuation of stimulants after a long period of use often leads to a temporary period of depression. Heavy amphetamine use has been linked to paranoid psychotic episodes and vivid hallucinations. However, amphetamine use itself does not appear to lead to long-term cognitive impairment. Long-term cocaine users can develop cognitive problems, particularly memory and concentration deficits, and impaired executive functioning.

MARIJUANA

Marijuana (cannabis) is often used for the subjective effects of relaxation and a decreased potential for conflicts. It is also known to distort perception of time and to reduce responsiveness. Long-term use of marijuana has been associated with apathy, under-achievement, and lack of motivation. However, in general the evidence linking

marijuana use to permanent cognitive changes is inconclusive.

HALLUCINOGENS

Hallucinogenic drugs distort perceptions and cause hallucinations. They include lysergic acid diethylamide (LSD), phencyclidine (PCP), mescaline, psilocybin mushrooms, and several newer drugs with hallucinatory and stimulant effects called *designer drugs*, (e.g., Ecstasy). In addition to profound effects on perceptions, hallucinogenic drugs affect responsiveness, learning, and judgment. Some users experience flashbacks, which are spontaneous vivid recollections of experiences that occurred while under the influence of hallucinogens. Flashbacks can occur long after the last use of the hallucinogen. Hallucinogen Persisting Perception Disorder is identified by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth edition (DSM-IV)* as the transient recurrence of disturbances in perception that are reminiscent of those experienced during one or more earlier hallucinogen intoxication. To meet criteria for the disorder these symptoms must not be due to current intoxication, they must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning, and they cannot be due to a general medical condition.

USE DURING PREGNANCY

Psychoactive drugs used during pregnancy affect the developing fetus. Prenatal exposure, particularly to alcohol but possibly to marijuana or stimulants, has been associated with cognitive impairments detectable early in the child's life and eventually resulting in developmental problems as well as school, social, and occupational difficulties.

See also **Imaging Techniques: Visualizing the Living Brain.**

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ENDOCRINE AND REPRODUCTIVE SYSTEMS

Many fundamental challenges remain in understanding the impact of alcohol and drugs on endocrine and reproductive function. Many factors can influence the degree to which drug or alcohol abuse can cause an abnormality of endocrine or reproductive function. These factors include (a) the amount and duration of consumption, (b) the route of illegal drug administration, (c) whether there is preexisting or concurrent damage to an endocrine/reproductive organ, (d) concurrent use of another drug, and (e) genetic risk for an endocrine disorder. Often our knowledge about these factors and how they interact with one another is more limited than what is known about the range of endocrine and reproductive dysfunction associated with the chronic consumption of alcohol and the abuse of illicit drugs.

Knowledge is also limited because some endocrine or reproductive consequences may become evident only when a laboratory (biochemical) test indicates an abnormal result. The absence of a physical sign or a clinical symptom may lead to the false impression that there is no endocrine or reproductive consequence. In addition, there are challenges in ascertaining whether the alcohol- or drug-abuse related endocrine or reproductive dysfunction is due to the drug itself or to the social context in which the drug is used. Finally, endocrine or reproductive disturbances may also occur from the consequences of withdrawal syndromes that occur when the ingestion of the drug or alcohol is stopped or reduced.

HYPOTHALAMUS/PITUITARY GLAND

The brain directly or indirectly influences most endocrine and reproductive function—specifically

by the functional interactions of the brain's hypothalamus and pituitary gland with the target endocrine organs. The hypothalamus produces pituitary-regulating hormones; all are peptides except one (dopamine). In response to each of these hypothalamic hormones, the pituitary releases a hormone, which influences the function of an endocrine or reproductive organ.

Alcohol. The anecdotal reports of changes in sexual function following alcohol consumption provided the stimulus for much of the research targeting hypothalamic-pituitary relationships because impairments here can often result in sexual dysfunction. Although acute alcohol use has been reported in public surveys to be associated with increased sexual drive and functioning, clinical and animal research has revealed major hormonal dysfunctions in chronic or heavy alcohol users.

Heavy alcohol use increases prolactin (PRL), the pituitary hormone associated with the preparation during pregnancy for breast milk secretion; however, chronic alcohol use inhibits the pituitary release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Both LH and FSH are important in regulating the sex hormones produced by the testes in males and the ovaries in females. Yet, the acute administration of alcohol does not produce significant changes in PRL, LH, or FSH serum levels.

Heavy alcohol consumption is associated with an increase in pituitary-secreted adrenocorticotropic hormone (ACTH), partly explaining the *pseudo*-Cushing's syndrome (moon-faced appearance, central obesity, muscle weakness) and the increased release of melanocyte-stimulating hormone (MSH), which possibly leads to increased skin pigmentation. Although there is no consistent effect of heavy alcohol use on the pituitary's release of thyroid-stimulating hormone (TSH) or growth hormone (GH), a rise in the blood alcohol level is associated with the inhibition of antidiuretic hormone (ADH) release from the posterior pituitary, resulting in increased urination.

Drugs. Complaints of derangements of libido (sex drive) and sexual functioning in opioid (heroin) addicts were among the first lines of clinical evidence to suggest the possible role of such narcotics in altering hypothalamic-pituitary functioning. Although most of what is known about drug-abuse related hypothalamic-pituitary abnormalities focuses on heroin use, the epidemic proportions of cocaine abuse and dependence in the 1980s have brought renewed scientific interest to this area.

Studies have shown that opioid use is associated with increased serum PRL without producing disturbances in serum GH or TSH levels, and cocaine use has been associated with both high and low PRL levels. The contradictory findings in the case of cocaine use might be attributable to the variations in patterns of cocaine use. Animal studies have shown that gonadotropin-releasing hormone (GnRH), released from the hypothalamus, did not stimulate PRL following acute cocaine administration, and it did not prevent acute cocaine-associated PRL suppression. Elevated levels of dopamine have been observed during acute cocaine administration, but chronic cocaine use may deplete dopamine.

Some investigators have reported a normal rise in TSH released by the pituitary in response to stimulation by the hypothalamic hormone called thyrotropin-releasing hormone (TRH) in patients receiving methadone therapy for opioid addiction. Others have observed a blunted TSH and PRL response following TRH administration in active heroin users.

Although normal basal LH secretion has been observed in cocaine abuse, opiate use is associated with decreased basal FSH and LH levels in males. In female heroin addicts, these low levels of the pituitary gonadotropins result in a consistently normal FSH response and a variable LH response following a GnRH challenge.

Some researchers have demonstrated normal functioning of the hypothalamic-pituitary-adrenal (HPA) axis in former heroin addicts who were maintained on methadone both long-term and only for a number of months. However, there is also evidence suggesting that methadone alters the normal biological rhythm of hormonal secretion.

SEX HORMONES

Diminished sexual drive and performance in opioid users have raised questions about the relationship between such narcotic drug use and disturbances in the levels of sex hormones. Although some reports

show no significant differences in serum testosterone levels between heroin addicts, methadone-maintained patients, and normal controls, other studies have not confirmed these results. Some researchers have reported that plasma levels of testosterone are consistently lower in active heroin addicts and in addicts who self-administer heroin in controlled research settings, and to be within the normal range in long-term methadone-maintained patients. Additionally, some evidence shows that plasma testosterone levels that are depressed under circumstances of heroin administration followed by methadone maintenance and then withdrawal gradually returned to preheroin-use levels. Alcohol consumption and cocaine use in excessive amounts are also associated with low testosterone levels.

Opioid effects on the estrogens produced by both men and women may be responsible for the clinical observations of sexual dysfunction. In the male heroin addicts studied, the plasma estradiol concentrations were either low or within normal ranges; in women, the plasma estrogens are low. A clear explanation of these observed derangements in plasma testosterone and estrogens is unknown. Female heroin addicts frequently experience cessation of or irregular menses. However, most regain normal menstrual function when stabilized on methadone and under these circumstances fertility seems unaffected. The anecdotal reports and, in limited cases, experimental evidence of the influence of marijuana on sexual function and sex-hormone levels are also inconsistent and confusing in humans.

The illicit drug-related disturbances discussed above suggest that the narcotic-related depressions in sex-hormone production of the ovaries and testes can occur because they reduce the pituitary's stimulation of these sex organs. However, this has not been a consistent finding.

REPRODUCTION AND PREGNANCY

Impotence, atrophy of the testes, infertility, and decreased libido are common complaints in male alcoholics. These observations are thought to be secondary to the direct effects of alcohol on testicular tissue, to an alcohol-associated decrease in sperm motility, and to an alcohol-related decrease in vitamin A and zinc. Both vitamin A and zinc are important in maintaining testicular tissue growth. In young women, alcohol abuse is associated with amenorrhea (loss of menses) and anovulation (lack of ovulation), and in chronic users, with early menopause. There is evidence that vaginal blood flow decreases as the blood alcohol level increases. There is evidence that alcohol is a protective factor against cardiovascular disease in postmenopausal women, by increasing estradiol production that normally decreases after menopause.

Despite these clinical observations, when rigorously investigated, there were no consistent changes in progesterone or testosterone. Consequently, it is difficult to determine whether these observations were due to alcohol-related liver disease, malnutrition, or the direct toxic effects of chronic alcohol use.

During pregnancy, alcoholism is associated with increased risk of spontaneous abortion (miscarriage), and the development of fetal alcohol syndrome (FAS) has been associated with drinking during pregnancy. FAS is a characteristic pattern of skin or facial abnormalities with growth and developmental impairments, which are believed to be related to alcohol's suppression of the sex hormone progesterone. The features of FAS may vary whereas fetal abnormalities associated with alcohol can be divided into the following four categories: (a) growth deficiency, (b) central nervous system dysfunction, (c) head and facial abnormalities, and (d) other major and minor malformations. In addition, abnormal development of the mammary gland was found to be associated with drinking before and during pregnancy. In animal studies, alcohol has been shown to decrease progesterone, which is important during mammary gland maturation, resulting in its decreased weight. The composition of milk produced is also affected in those that consume or have consumed alcohol. In animal studies milk production is decreased and it contains less protein and lactose with an increase in lipids.

ADRENAL GLANDS

Our understanding of the relationship between opioid drug use and the functioning of the adrenal gland is based on incomplete and often contradictory information. Some scientists have published reports of normal plasma levels of cortisol (a hormone released from the adrenals) during heroin use and withdrawal, under research conditions of

heroin self-administration, and during methadone-maintenance treatment. In other studies, researchers have found low plasma cortisol and ACTH levels in heroin users. In methadone-treated patients, ACTH produced by the pituitary stimulates the adrenal gland to produce cortisol. In another study, there was a decreased plasma cortisol response to stimulation with intravenous cosyntropin (an ACTH-like substance) in methadone-treated patients. There are also reports of low normal or subnormal plasma cortisol levels in heroin users and disturbances in the daytime cortisol secretion from the adrenal gland in methadone-maintained patients.

The variable findings from these studies may be attributed to differences in the types of drugs used, in the state of stress-associated drug withdrawal, in patterns of drug use, in study design, or to a combination of these and other as yet unknown factors. There is also the well-known problem of inaccurate ACTH measurement, often resulting in falsely low values.

CARBOHYDRATE METABOLISM

The opioids are virtually the only class of *illegal* drugs for which there is information about the pharmacologic effects on serum glucose levels. There are long-standing reports of opiate-associated hyperglycemia (elevated blood sugar concentration), but the mechanisms explaining these findings are not fully understood. In association with chronic opioid use, there are reports of both low levels of serum glucose and high levels of insulin. The conflicting results of some investigations may be due, in part, to differences in study design (e.g., the nutritional state of the research subjects, the amount of glucose used in clinical studies, or the time(s) of glucose administration).

To briefly review the regulation of glucose control: The pancreas, an endocrine organ located in the upper abdomen, plays a central role by secreting glucagon to raise serum glucose levels and by secreting insulin to lower serum glucose levels. After the discovery of endogenous opioid peptides in the human pancreas, subsequent research provided information that one such endogenous opioid, beta-endorphin, stimulates the secretion of glucagon and a biphasic rise in insulin concentration. This may, in part, explain the observations of both elevated and reduced serum glucose levels in heroin users. Whatever the nature of the mechanism, glucose metabolism is deranged in both heroin and methadone users by a direct or indirect parameter of serum glucose regulation.

The alcohol-related aberrations of carbohydrate metabolism are also quite complex. Some investigators have demonstrated that acutely administered alcohol may result in a reversible and mild resistance to the glucose-lowering effects of insulin, perhaps explaining the observations of a rise in glucose following alcohol use. Increased alcohol consumption decreases glucose production by creating more triglycerides and lactic acid in the body during alcohol metabolism. In individuals who are fasting, alcohol administration can lead to a severe depression of serum glucose, primarily by reducing its production in the liver. Serum glucose levels are also lower in chronic alcohol users with concurrent alcohol-related liver disease. Nevertheless, serum levels are elevated in alcoholics with concurrent alcohol-related destruction of the pancreas. Even without other concurrent diseases, alcohol consumption may result in either no changes or in minimal to mild elevations or reductions in serum glucose. There also appears to be a difference in alcohol's effects on glucose according to the sex. In animal studies, it appears that females tend to be affected more by alcohol and, with chronic ingestion, produce less glucose.

THE THYROID GLAND

Located in the anterior aspect of the neck, the thyroid gland secretes thyroxine (T_4) and other hormones whose principal purpose is to regulate the metabolism of other tissues in the body. TSH, which is produced by the pituitary, controls the thyroid production of T_4. Therefore alterations in thyroid function can be the result of problems directly involving the gland or disruptions in the TSH-mediated control of the thyroid gland.

Despite the frequency, duration, or amount of use, it appears that there are no clinical signs or symptoms of thyroid dysfunction in chronic heroin or alcohol users. Disturbances in biochemical indices (laboratory tests) of thyroid function are, however, not uncommon in opiate or alcohol use. In heavy drinkers, the total T_4 is decreased while the

amount of biologically available T_4 (free T_4) and other indices of thyroid function are normal. An increase in thyroid volume has been observed in both women and men with the increase of alcohol consumption.

In active heroin users or during heroin withdrawal, total T_4 levels are increased in association with normal, subnormal, or high levels of other parameters of thyroid function. In addition T_3 (triiodothyronine) levels have been found to be elevated in heroin users. In methadone-maintained people, there are reports of normal and slight-to-significant increases in total T_4 in conjunction with increased levels of thyroxine-binding globulin (TBG), a protein that binds thyroid hormones in blood. Interestingly, methadone maintenance is associated with a correction of these biochemical disturbances.

There are a number of possible explanations for the biochemical derangements observed during opiate use. The total T_4 is increased whenever there is an increase in TBG, to maintain an adequate range of biologically active T_4. Perhaps the increase in total T_4 is the result of a direct opiate-induced elevation of TBG. It is also possible that the altered liver function seen in chronic heroin and alcohol users is responsible for TBG abnormalities leading to disturbances in T_4 levels. Finally, it is possible that opiate-related or alcohol-related disturbances are due to a combination of the above mechanisms as well as to some other still undefined processes.

BONE METABOLISM

The observations of increased fractures sustained by alcoholics have prompted investigations about the role that alcohol may play in disturbances of the structure and the mechanical properties of bone. Some studies have shown reduced bone mass in alcoholics, while others have reported decreases in compact and trabecular bone mass—a condition called osteoporosis. Some of these disturbances in new bone formation may be mediated by alcohol's impairment of calcium and Vitamin D metabolism, both of which are crucial to bone metabolism. In a human study, lower calcium blood levels were found in individuals that consumed alcohol, resulting from a greater excretion of calcium from their bodies. In addition, alcohol impairs bone formation by inhibiting osteoblasts, the cells responsible for such formation.

Nevertheless, there does remain considerable doubt as to whether the bone complications are because of alcohol itself or because of alcohol-related liver disease, of malnutrition, or of a host of other potential factors. Chronic liver disease unrelated to alcohol has also been a cause of osteoporosis and other bone diseases.

IMPORTANCE TO PUBLIC HEALTH

The endocrine and reproductive consequences of drug and alcohol abuse are extensive and profound. Both drug and alcohol abuse result in clinically significant derangements in many different endocrine systems. Although knowledge about the dimensions of such disturbances to endocrine and reproductive function slowly increases, the scientific mechanisms accounting for these observations remain to be elucidated. Given the role of alcohol and drugs in society, however, the spectrum of related endocrine and reproductive complications can be expected to expand and, thereby, increase in public-health significance.

See also **Alcohol: History of Drinking (International); Alcohol: History of Drinking in the United States; Alcoholism: Abstinence versus Controlled Drinking; Cocaine; Complications: Liver (Clinical); Dopamine; Heroin; Methadone Maintenance Programs; Opiates/Opioids; Opioid Complications and Withdrawal; Risk Factors for Substance Use, Abuse, and Dependence: Drug Effects and Biological Responses; Sexuality and Substance Abuse.**

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IMMUNOLOGIC

This article describes the basic and clinical immunologic aspects of alcohol and drug abuse.

ALCOHOL

The physiological characteristics of alcohol (ethanol) allow it to interfere with the functions of immune cells. Alcohol is able to completely mix with water and, to some degree, is fat soluble. It crosses membranes by diffusion across a concentration gradient, going from high to low concentrations. Historically, alcohol has been associated with lower host resistance and increased infectious diseases. For example, alcoholism has been closely associated with lung abscesses, bacteria being found in the blood, abdomen infection, and tuberculosis. Although these infections might be a result of malnutrition or poor living conditions, prolonged consumption of alcohol also results in alterations of immune responses, seriously impairing the body's normal host defense not only to invading microbes but also to its defense against cancer cells.

These disruptions are the combined result of direct toxic effects on the immune system and indirect effects such as malnutrition, oxidative stress, endocrine changes and the complications of liver disease. The alcoholic's predisposition to extracellular and intracellular infection indicates the effects of alcohol consumption at the local, humoral immunity (includes antibodies and B cells), and cellular levels, inhibiting immune response and host defense. Some evidence suggests that disrupted regulation of the neuroimmune-endocrine networks may be a major risk factor for the development of alcohol-induced immunosupression, leading to the collapse of host defense. Bidirectional communication can occur between the immune and neuroendocrine systems. Accordingly, stimulated lymphoid cells send signals mediated by soluble mediators (termed *cytokines*) and other immune products to inform the central nervous system about the activity of the immune system. Neuroendocrine molecules, in turn, may complete a feedback loop by modulating neural output. Thus, effective feedback communications between the endocrine and the immune systems may be crucial to the host's response.

Clinical and experimental studies indicate a relationship between excessive alcohol use and compromised immune responses (Szabo, 1997). Human studies have shown that chronic alcohol ingestion is associated with abnormalities of both

humoral and cellular immunity (Diaz et al., 2002; Szabo, 1997). These abnormalities include a depression of serum bactericidal (body's ability to kill bacteria) activity, alterations of immunoglobulin production, leucopenia (abnormally low number of leukocytes), defects in Chemotaxis (movement based on a chemical, can be attractant or repellent), decreased antigen trapping and processing, and decreased T-cell mitogenesis (mitosis). The clear association between alcoholism and infections such as tuberculosis and listeriosis (has a wide range of effects from being sick to Meningitis and is caused by L. Monocytogenes and is usually acquired from food) indicates defective functioning of cell-mediated immunity. A study has linked alcohol abuse and deficient T-cell responsiveness (Szabo, 1997). Skin-test reactivity using purified protein derivative and dinitrochlorobenzene has also demonstrated poor responses in alcoholics with liver disease. Natural killer (or NK) cell activity is impaired in acute alcohol intoxication and in chronic alcoholic liver disease. NK cells are programmed to recognize and destroy abnormal cells, such as virus-infected or tumor cells. Some researchers have speculated that decreased NK cell activity may be intimately involved in the increased incidence of tumors in alcoholics.

Having animals ingest alcohol also has a profound effect on decreasing the weight of their peripheral lymphoid organs as measured by a decreased number of thymocytes and splenocytes (T cells in the thymus and spleen). In mice, alcohol use produces thymic and splenic atrophy and alterations in the circulating lymphocytes and lymphocyte subpopulations, as well as alterations in cellular and humoral immunity and impaired cytokine production. Also impaired by dietary alcohol are antibody-dependent cellular toxicity, lymphocyte proliferation, B-lymphocyte functions, and cytokine production by lymphoid cells (in the lymph and lymph nodes). Thus, alcohol-induced immunosuppression may render alcoholics more susceptible to tumorigenesis (tumor development) and infection.

Alcoholics are susceptible to infections by bacteria such as Listeria monocytogenes, Vibrio vulnificus, Pasteurella multocida, Aeromonas hydrophilia, Klebsiella pneumoniaeand legionalla pneumophila and Mycobacterium tuberculosi. The severity of these infections has raised the possibility of a neutrophil (white blood cell) and macrophage (cells in the innate immune system that kill pathogens by phagocytosis/swallowing them) abnormality in these patients. The proper functioning of neutrophils is critical for host defense against microorganisms. Neutrophils are the chief phagocytic (kill by swallowing) leukocyte of the blood; they are short-lived cells having a life span of approximately four days. Their production is a tightly regulated process centered in the bone marrow. Chronic alcoholics have often been noted to be leukopenic (low levels of leukocytes). The toxic effect of alcohol is now believed to be caused by the depression of the T-cell-derived colony-stimulating factor rather than to direct suppression of myeloid (bone marrow) precursors secondary to bone marrow toxicity.

Neutrophils (cells of the innate immune system that use phagocytosis) must recognize the invading pathogens, engulf them, and destroy them using a number of killing mechanisms, which include adherence, chemotaxis, locomotion, phagocytosis, and intracellular killing. Several functions of neutrophils are affected by alcohol in vitro, including impairment of chemotaxis, decreased migration of neutrophils within vessels, altered adherence to nylon fibers in vitro, impaired phagocytosis, and decreased intracellular killing of bacteria. In humans with advanced cirrhosis from chronic (prolonged and excessive) ingestion of ethanol and impaired phagocytic capacity, decreased metabolic activity was observed in the liver's reticuloendothelial system; there also were impairments of neutrophil chemotaxis, bacterial phagocytosis and killing, and alterations of neutrophil-antigen expression. Neutrophil dysfunction is therefore responsible for aggravating the susceptibility to secondary infections seen in alcoholics.

The balance of the cellular and humoral immune system response to antigens is controlled by communication between immunocompetent (healthy cells of the immune system) cells. They are regulated to a great extent by cytokines produced mostly by T-helper cells and macrophages. Cytokines and biologically active polypeptide intercellular messengers regulate the growth, mobility, and differentiation of leukocytes. Thus, cytokines have extremely important roles in the communication network that links inducer and effector cells to immune and inflammatory cells.

Given that any perturbation in the tightly controlled cytokine regulatory system can result in immune alterations modifying host resistance to infectious disease and cancer, the influence of alcohol consumption on cytokine secretion has been investigated considerably. Several studies have indicated a correlation between circulating levels of macrophage-derived cytokines and disease progression during chronic alcohol consumption (Szabo, 1997). Increased plasma concentrations of tumor necrosis factor have been observed in cases of alcoholic liver disease and, interestingly, related significantly to decreased long-term survival. Plasma interleukin-I (also a cytokine) is also significantly increased in these patients (relative to healthy controls) but does not correlate with increased mortality. Additionally, higher levels of the cytokines interleukin-6, interleukin-8, and interleukin-10 have been found in chronic heavy drinkers, with a reverse in levels possible after the cessation of drinking.

In alcohol-fed mice, researchers found that, compared to controls, production of all cytokines was suppressed by chronic alcohol consumption, suggesting general immunosupression. The elevated levels of cytokines in some animals with murine (mouse) AIDS were, however, increased further by alcohol ingestion as compared to controls, which reflected the alcohol-induced aggravation of some AIDS symptoms. Similarly, those cytokines suppressed by murine AIDS were further suppressed by alcohol. Thus, alcohol exacerbated their immune dysfunction. In simians (higher primates), animals with HIV infection had increased virus replication when exposed to alcohol. There was increased proliferation of cells isolated from humans with HIV, when they were treated with alcohol in vitro. Several pathways may be involved in mediating the interaction between the endocrine system and the immune system. Some findings indicate that the pituitary peptide hormones can directly influence immune response. In addition, when a neurotransmitter is released in lymphoid tissues, it may locally modify the functional properties of lymphocytes and the release of cytokines.

In human studies on the effects of alcohol, hormone levels and immune responses to monitor changes of immune response and neurotransmitters are usually detected in serum. Since the serum levels of these parameters cannot accurately reflect the local situation in the lymphoid organs or tissues, some results from these studies, therefore, could be misleading. No animal model for alcohol studies can mimic the complications of alcoholic liver diseases often observed in humans. Furthermore, because individual animals differ in their hormonal status, even within the same strain of animal, and it is difficult to define the hormone status of animals, some results from animal studies may also be misleading. Therefore, further research is needed as of 2008 on the mechanism of alcohol's effects on the neurological system at the cellular and systemic levels. Similarly, research on the interaction between the endocrine and immune systems should continue to enhance the understanding of the complex changes caused by the direct and indirect effects of alcohol consumption.

COCAINE

Cocaine acts directly on lymphoid cells (the lymph and lymph nodes) and indirectly modulates the immune response by affecting the level of neuroendocrine hormones. The first studies about the impact of cocaine use on the immune response were initiated because epidemiological data demonstrated a high prevalence of acquired immunodeficiency syndrome (AIDS) in polydrug users. Depending on the different administration routes, the plasma levels of cocaine in humans appear to be in the range of 0.1 to 1 micrograms per milliliter (μg/ml). Such concentrations last only for thirty to sixty minutes and then decline because of cocaine's short biological half-life (about 1 hour). Consequently, the direct effects of cocaine and its metabolites on immune cells should occur only during a short time, except in heavy cocaine users who use the drug several times a day every day. Besides the direct effects on immune cells, cocaine could indirectly affect the immune response via its impact on the neuroendocrine system, and both have been shown (Pellegrino, 1998; Watzl, 1990).

Short-term exposure of mice to cocaine by daily intraperitoneal (within the abdominal cavity) injection for fourteen days reduced body, spleen, and thymus weight in the animal. Cocaine increased the responsiveness of lymphocytes to mitogens (cell proliferation initiators) and the delayed hypersensitivity responsiveness, but it suppressed the antibody response. Many animal studies, however, suggest

that the immune system requires continuous exposure to cocaine to demonstrate its suppressing or stimulating effects and may also be dependent on the dose (Pellegrino, 1998). After a single dose of cocaine (0.6 mg/kg), non-habitual cocaine users showed a significant stimulation of natural killer cell activity, which is vital to defend against cancers. The level of natural killer cells was also increased, but the levels of T-helper and suppressor cytotoxic cells, B cells, and monocytes were not elevated. In contrast, T cell levels were found to be decreased in newborns that were exposed to cocaine through maternal use during gestation.

Cocaine causes neuroendocrine-mediated effects on the immune response. It stimulates the brain's hypothalamus to increase secretion of beta-endorphin. As a result of cocaine administration, beta-endophin binds to opioid receptors on monocytes and lymphocytes and exerts multiple stimulating and suppressing effects on these cells, including secretion of immunoregulatory cytokines. The net outcome of the reactions related to the immune response of the host is difficult to assess because of other possible determinants of these interactions (such as the psychological and social state of the cocaine user).

There are other mechanisms that might operate to mediate cocaine-induced Immunomodulation (T cells secreting cytokines and enhancing or decreasing this activity), including nutritional deficiencies and their impact on lymphoid cells. As early as 1870, the French physician Charles Gazeau suggested that coca leaves might be used to suppress the appetite. With food deprivation, which is common in circumstances of habitual drug use, the self-administration of cocaine by rats increased. Although data indicate a poor nutritional status for cocaine users, no study has as of 2008 assessed the nutritional status of drug users as it contributes to a compromised immune competence. Cocaine clearly modifies hormones with immunoregulatory properties via neurological effects. In addition, malnutrition could be a factor in cocaine use, resulting in altered disease and tumor resistance. Intravenous use of drugs, including cocaine, is associated with the transmission of human immunodeficiency virus (HIV), and ultimately the development of AIDS. Immunomodulation by cocaine after HIV infection could accelerate disease development as well as decrease overall resistance to a variety of pathogens found frequently in intravenous drug users. One of the proposed mechanisms for this lowering of the immune response occurs through the high levels of TGF-β (a cytokine) found in cocaine users with HIV, which will decrease the immune system's ability to respond and allow virus replication.

TOBACCO

Although it is well known that the use of tobacco is a major health hazard, millions of Americans continue to smoke and the popularity of smokeless tobacco is on the rise. Tobacco use is the chief cause of lung cancer in smokers of tobacco and is strongly linked with the oral cancers of those who use chewing tobacco or snuff.

The pulmonary alveolar macrophage (PAM) is the cellular component of the immune system comprising the first line defense of the lung, offering protection against inhaled particles, including irritants and microbial invaders. Because PAM has exposure to both the bloodstream and the atmosphere, it is uniquely suited to perform its protective functions, which include clearance of foreign material, immune modulation, and modulation of surrounding tissue. There is general agreement that the number of PAMs in smokers' lungs is increased two to twenty times above that found in the lungs of nonsmokers. It also appears that there is a difference in the morphology and certain aspects of the function of alveolar macrophages between the two groups. In general, PAMs from smokers are larger, contain more lysosomes and lysosomal enzymes, and are more metabolically active than those from nonsmokers, suggesting that they may be in a chronically stimulated, more active state. These enlarged PAMs might lead to the inference that there would be greater phagocytotic capacity in the lungs of smokers, resulting in increased clearance of foreign matter. However, the responsiveness of smokers' macrophages to foreign bodies or bacteria was equal to or less than that of non-smokers, leading researchers to conclude that chronic stimulation of PAMs by cigarette smoke may be harmful rather than beneficial to the immunocompetence of the lung.

There is some disagreement as to whether smoking affects the phagocytotic and bactericidal activity of PAMs. The question of whether tobacco

smoke alters the tumoricidal (tumor killing) ability of PAMs has not yet been answered. Thus, the relationship between cigarette smoking, neutrophil accumulation in the lung, and lung destruction continues to be researched. It is known that particles from cigarette smoke are present in the PAMs of smokers, and researchers have found that the PAMs of cigarette smokers release a potent chemotactic factor for neutrophils (chemotactic factor: chemicals that can recruit or keep away the neutrophils), whereas those of nonsmokers did not. Therefore, cigarette smokers had an increased number of neutrophils in the lavage fluid (cells taken through needle aspiration, can be cells from the breast/milk duct in the ductal lavage, or can be broncheoalveolar cells [King et al., 2003; Wang et al., 2005]) in the lung biopsy tissue as compared to nonsmokers. Neutrophils store and release elastase, an enzyme that can break down connective tissue, a process that is implicated in the development of certain lung diseases. Smokers' lungs are exposed to a large chronic burden of elastase from neutrophils, which may predispose them to lung destruction.

A number of animal and human studies comparing blood samples of smokers and non-smokers have indicated that smokers have altered immunoglobulin levels (Prescott, 2008). Elevated levels of immunoglobulin E (IgE) were present in a high proportion of the smoke-exposed animals but in none of the control animals. Studies on human subjects have also revealed that IgE levels were higher in smokers than in nonsmokers. A study of coal workers showed that both mining and nonmining smokers had depressed serum IgA and IgM levels as compared with similar groups of nonsmokers. A disturbing finding in relationship to increased immunoglobulin levels in smokers is the effect that maternal smoking may have on the fetus. In newborn infants of mothers who smoked during pregnancy, IgE was elevated three-fold. Tobacco smoke affects fetal immunoglobulin synthesis, stresses the fetal immune system, and can predispose the infant to subsequent sensitization. It has been estimated that maternal smoking causes 34 percent of the reported asthma in childhood.

Natural killer cells, thought to serve important anti-tumor and antiviral functions in the body, have been found to be decreased in adult smokers as well as in cord blood from infants whose mothers either smoked during pregnancy or inhaled second-hand smoke (Watson & Witten, 2001). Studies of the white blood cells called basophils in the peripheral blood indicated that there are alterations linked to tobacco smoking as well.

Smoking has also been found to be associated with autoimmune diseases. Tobacco use and rheumatoid arthritis have been linked, with a higher risk associated with those with greater tobacco consumption. Smoking can accelerate disease progression as TNF-α (Tumor Necrosis Factor) (a cytokine) levels are elevated in smokers with rheumatoid arthritis. Smoking also increases the odds for developing the autoimmune disease systemic lupus erythematosus (SLE). One plausible way that this can occur is by smoking, causing DNA damage and creating anti-dsDNA antibodies, levels of which can help to identify active disease in patients with SLE.

In considering the effect that tobacco use has on immunocompetence, other confounding variables must also be accounted for, including genetic factors, pre-existing disease, and nutritional status. Smoking has been observed to cause deficiencies of Vitamin C, beta-carotene (Vitamin A), and other nutrients that have important functions in protecting immunity.

Tobacco smoking causes deleterious effects on the pulmonary and systemic immune systems of experimental animals and humans. Aspects of both cell-mediated and humoral immunity are affected. It is often difficult to compare studies directly because of the variability in smoking behaviors and the differences among tobacco products. Although it is expected that heavy smoking causes the most amount of immune system damage, that does not mean light to moderate smoking is safe. Thus, if some alterations due to smoking are reversible, it is not yet known whether long-term smoking may cause the impairment of the immune system to become permanent. Further, simultaneous exposure to other air contaminants or air pollution may exert damaging synergistic effects on local or systemic immune defenses.

MORPHINE AND OTHER OPIOIDS

Several studies have revealed a parallel between morphine abuse and immune inhibition (Wang et al., 2005). In vitro studies have shown that

polymorphonuclear cells and monocytes from patients subjected to morphine treatment were severely depressed in their phagocytic and killing properties as well as in their ability to generate superoxide. Opioid addiction also caused alterations in the frequencies of T-cells and null lymphocytes in human peripheral blood.

There is convincing evidence of the presence of opioid receptors on various types of human immune cells. The presence of opioid receptors on immune cells may allow for modulation of specific immune functions in the presence of exogenous (not a natural part of the body, from an outside source) opiates. Various administration schedules for opioids were shown to potentiate infection by *Klebsiella pneumoniae*, *Streptococus pneumoniae*, and *Candida albicans.* The increased susceptibility was partly due to decreased reticuloendothelial-system activity as well as a reduction in the number of phagocytes, not by a direct cytotoxic effect of the opioid. In addition, susceptibility to HIV and tuberculosis has been associated with opioid use.

Chronic administration of morphine has also inhibited a primary antibody response of mice as B cell levels have been found to be depressed when the mice were exposed to morphine. These effects were worsened by naloxone (a non-addictive analog of morphine that blocks opiate receptors), indicating that morphine inhibits the immune system in a specific manner—via its interaction with opioid receptors. Other studies in animals such as rats and monkeys have shown that morphine can decrease NK cell activity, perhaps reducing resistance to tumors.

Such changes, which can also include morphine suppression of spleen and body weight, show evidence of a significant reduction in immune function.

MARIJUANA

Several approaches have been used to study the effects of marijuana or its active component, tetrahydrocannabinol (THC), on the human immune system. These include using cells isolated from chronic marijuana smokers, from volunteers who have been exposed only to marijuana smoke or from non-exposed donors whose cells are exposed to THC in the laboratory. A survey of chronic marijuana smokers showed a depressed response of their cells to stimulation with mitogens (substances that cause cell division).

Several studies have shown that marijuana smoking and THC is immunosuppressive (Klein et al., 1997; Klein et al., 2000; Tashkin et al., 2002). Immune alterations have been associated with marijuana or THC, including significantly reduced serum IgG levels in chronic smokers; inhibition of natural killer cell activity; inhibition of phagocytic activity through altered macrophages; elevation of serum IgD levels; increased neutrophils; and reduced T-cell numbers. THC also inhibited DNA-, RNA-, and protein synthesis in stimulated human lymphocytes.

Studies performed in animals have produced more consistent findings than those in humans. In most cases, THC is associated with suppression of various immune parameters. Mice that have been exposed to THC are more susceptible to infections through *Legionella pneumophila* and *Candida albicans.* The greater the consistency observed in animal studies probably reflects the influence of genetic factors, consistent dosage levels, diet, and other conditions that can readily be controlled in animal studies.

Animal studies have thus provided strong evidence of the immunosuppressive effects of THC. Such effects have been clearly demonstrated by animals, who when exposed to THC, were more susceptible to infections than non-exposed animals (Cabral & Pettit 1998). In mice and guinea pigs, THC has also exacerbated viral infection and reduced resistance to bacterial pathogens.

See also **Alcohol and AIDS; Alcohol: Chemistry and Pharmacology; Cocaine; Marijuana (Cannabis); Opiates/Opioids; Tobacco: Medical Complications; Tobacco: Smokeless.**

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LIVER (CLINICAL)

The liver is the largest internal organ of the human body, normally weighing about 3.3 pounds (1.5 kg). It occupies the right upper quadrant of the abdominal cavity just below the diaphragm. As befitting its anatomical prominence, its function is essential to maintain life. Surgical removal of the entire liver from any animal (including humans) would result in the animal's falling into a coma shortly thereafter and then dying. The absence of a certain critical mass of functioning liver tissue is incompatible with life. While the human liver has a remarkable resilience and regenerative capacity after injury or illness, this is true only up to a certain point. If illness damages the liver beyond the point of no return, the person dies.

The liver has a multitude of complex functions and is justly called the laboratory of the human

body. It secretes a digestive juice called *bile* into the intestine, called bile; it produces a number of essential proteins, clotting factors, and fatty substances; it stores and conserves energy-producing sugars; it detoxifies both internally produced and external toxins and drugs that would otherwise be poisonous to the human organism—just to name some of its important functions.

What can seriously jeopardize this very important organ and consequently the well-being and survival of the individual? For one, there are diseases—both congenital and acquired—over which a person has little or no control, such as some genetically determined and developmental abnormalities, circulatory liver problems, certain tumors, and infections. A very large part of *hepatology* (the technical term to describe the study and treatment of liver diseases) is, however, devoted to liver problems created by a peculiar human behavior—the abuse of alcohol and drugs. Whereas discussions as to whether alcoholism and drug abuse are truly self-inflicted problems elicit a variety of opinions, the liver disease that results from substance abuse in a given individual could have been avoided if the substance-abusing behavior had not occurred. Beyond the psychosocial consequences of substance abuse, diseases of the liver (and brain) represent the major complications of alcohol and drugs. The morbidity (disease incidence) and mortality (death incidence) from alcoholic and drug-induced liver injury are very high. In the scientific literature, it is well established that the mortality from alcoholic liver disease is correlated with per capita alcohol consumption; in fact, the prevalence of alcoholism in a given society has been calculated from liver mortality statistics. While alcohol is a direct liver toxin, most of the other commonly abused psychoactive substances are generally not known to affect the liver directly to a great extent. Their major contribution to liver morbidity and mortality is via exposing people to viral hepatitis, a potentially fatal disease.

ALCOHOLIC LIVER DISEASES

This section discusses the range of alcoholic liver diseases. The interrelationship between them is illustrated in Figure 1.

Alcoholic Fatty Liver. Fat accumulation in the liver is an almost universal response to excessive alcohol consumption. It occurs in the majority of heavy drinkers. How and why fat accumulates in liver cells is complicated and not completely understood; however, its presence may be observed. If a piece of biopsied liver tissue from an alcoholic is examined under the microscope, the observer will see that many liver cells are loaded with big bubbles consisting of fat, almost totally occupying the cell. In most cases, this fatty change does not matter much as far as the patient's health is concerned. It is an almost invariable response to too much alcohol consumption and an early warning. The person who has nothing worse than an alcoholic fatty liver may not feel sick at all, and only if a biopsy is done can the fatty liver be diagnosed. The doctor may feel an enlarged liver by palpation (pushing on the abdomen to feel the internal organs), which may be a bit tender. The laboratory test may show a slight elevation in the blood of some liver enzymes, best known by their initials: SGOT (or AST) and SGPT (or ALT). These enzymes are elevated because some of them tend to leak out of the fatty liver cells into the blood.

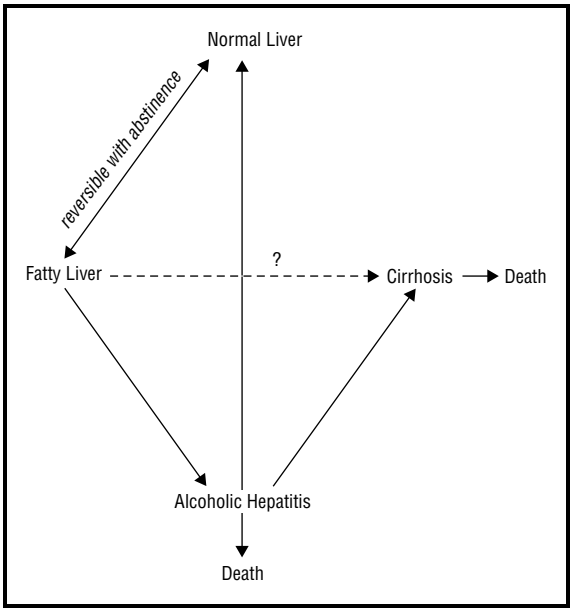


Figure 1. Interrelationships between various forms of alcoholic liver disease. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

If a person stops drinking, the fat disappears from the liver cells, the swelling subsides, and the AST and ALT levels become normal. The two-way arrow in the diagram of Figure 1 indicates that fatty

liver is reversible with abstinence, and the condition may fluctuate back and forth between normal and fatty liver with abstinence and drinking, respectively. Thus, fatty liver in itself is not likely a serious situation; it is an early warning that the liver does not respond well to alcohol and that its condition may worsen. There was a time when fatty liver was regarded as a precursor of the end-stage liver disease called cirrhosis (indicated by the broken arrow and question mark on Figure 1), but most physicians do not now believe that this direct connection exists.

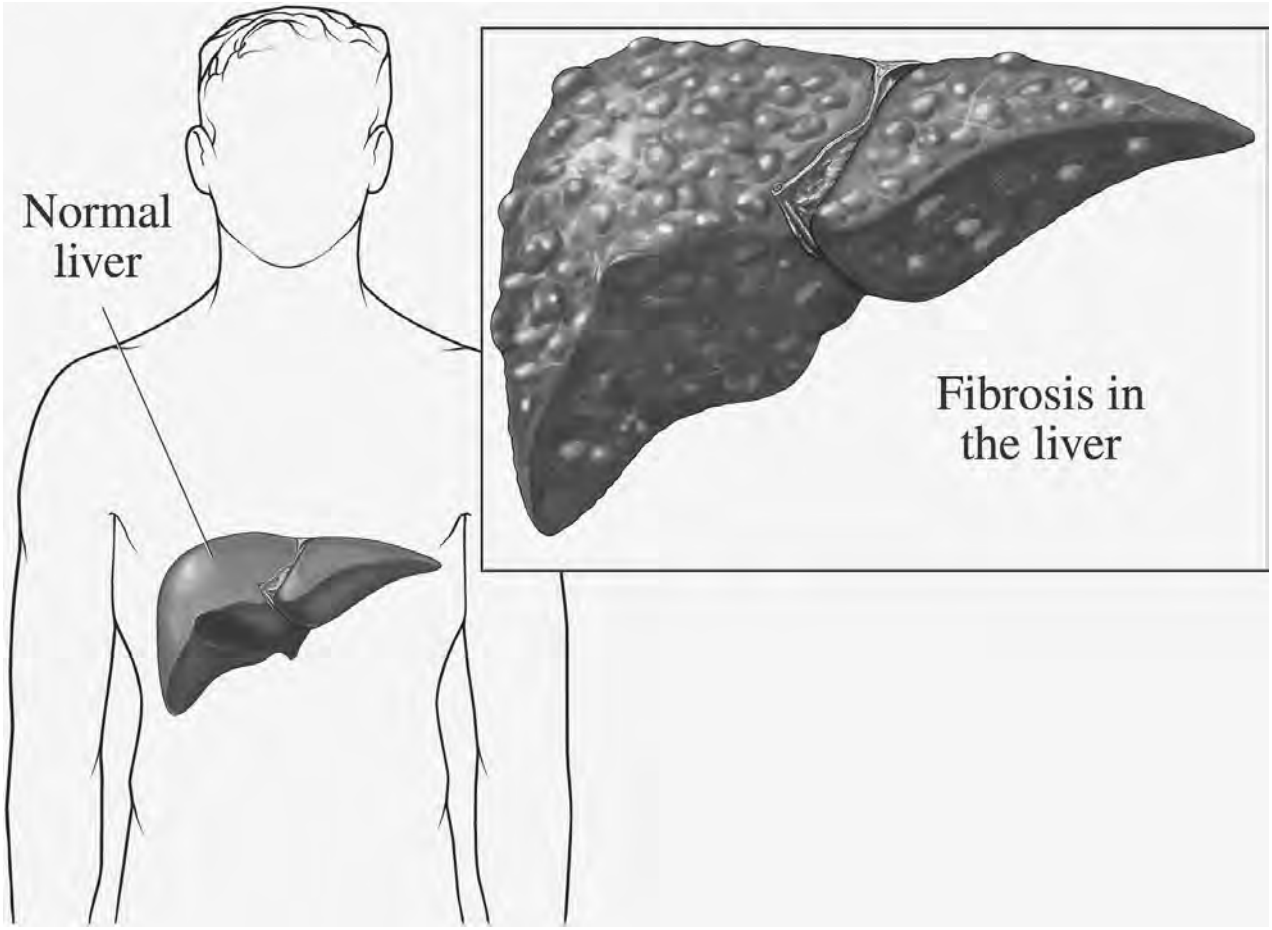
Alcoholic Hepatitis. Alcoholic hepatitis is a potentially more serious form of alcoholic liver disease. A certain proportion of alcoholics, in addition to accumulating fats in their livers when drinking, will develop inflammation (hepatitis means liver inflammation) consisting of an accumulation of white blood cells, the death (necrosis) of some of the liver cells, and the presence of some very characteristic material called *Mallory bodies.* Again, all these changes can be seen under the microscope in a biopsied piece of tissue.

The clinical picture of alcoholic hepatitis varies. At one extreme is the person who feels perfectly well and only the biopsy could indicate that something is wrong. At the other extreme is the dying patient with a swollen and painful liver, jaundice (a yellowing of the entire body from bile pigment leaking into the blood), fever, and disturbed consciousness. Between these extremes are people with varying degrees of illness; for example, with or without some jaundice, with or without pain and fever. The white blood cell count is usually elevated. The bilirubin (bile pigment) level may be elevated in patients who have turned yellow (a pale to deep mustard). The liver enzymes are higher than normal in the blood because they leak out of the inflamed liver cells. However, these values are not as high as in viral hepatitis. In alcoholic hepatitis AST (SGOT) is higher than ALT (SGPT). This finding helps to distinguish alcoholic hepatitis from viral hepatitis, which is difficult to do at times. In viral hepatitis not only are the absolute enzyme values higher, but the ratio is reversed: ALT is higher than AST.

Thus, the outcome of alcoholic hepatitis can be death (worst scenario) or recovery (best scenario), as shown on Figure 1. Even if the patient does not die in a given episode, repeated episodes of drinking and alcoholic hepatitis can lead to the last stage of alcoholic liver disease: cirrhosis.

Alcoholic Cirrhosis. In terms of histology (tissue damage) alcoholic cirrhosis is an end-stage disease: a cirrhotic liver cannot become normal. In Figure 1, there is no arrow between cirrhosis and normal liver. Clinically, cirrhosis is a serious disease, potentially fatal, but not inevitably so. Alcoholism, while not its only cause, is by far the most common. Under the microscope a cirrhotic liver shows a disorganized architecture: the dead (necrotic) liver cells have been replaced by scar tissue. The liver tries to repair itself. In a somewhat haphazard fashion it attempts to produce new liver tissue in the form of nodules, which are separated from each other by scar tissue. These newly formed liver nodules may indeed sustain liver function and thus life for a time, but at a price: the liver's blood circulation is mechanically compressed. Thus, pressure increases in the blood vessels leading to the liver. Some of these overloaded blood vessels, especially those on the border of the stomach and esophagus (called esophageal varices), can rupture at any time, causing a major hemorrhage.

Patients in the cirrhotic stage of alcoholic liver disease present their symptoms in various ways. Some of them look quite normal; only the biopsy will reveal the presence of cirrhosis. Others are jaundiced, the yellow color from bile pigment leaking out of the damaged liver into the blood, thus staining the skin and the whites of the eyes. Still others have large fluid accumulations in their extremities (edema) or in their abdominal cavity (ascites). The latter may make these patients—men or women—look like they are nine months pregnant. Some may vomit blood because of the hemorrhaging. In most advanced cases, there is just not enough functioning liver tissue left; the liver no longer can perform its laboratory function, and the person slips into a coma and may die. When cirrhotic patients are examined by doctors, their livers do not feel smooth but bumpy from the nodules that have formed. At first the liver may be swollen and enlarged, but in the later stages it shrinks. The ultrasound picture suggests a patchy, disorganized liver architecture. The spleen may enlarge from the increased pressure in the blood vessels. The liver enzymes (AST and ALT) may be moderately



Cirrhosis of the liver. NUCLEUS MEDICAL ART/PHOTOTAKE

elevated as in other forms of alcoholic liver disease, but this elevation has no prognostic importance. More ominous signs pointing toward severely compromised liver functions are the following: a decrease in blood level of albumin (an important protein manufactured by the liver), deficiency in blood-clotting factors that are also made in the liver, and the presence of anemia (low hemoglobin and red blood cell count).

Causes of Death in Cirrhosis. Ascites (fluid accumulation in the abdomen) is very uncomfortable and unsightly but by itself usually does not kill, unless infection develops, which is always a threat. Generally, cirrhosis compromises the immune system, rendering cirrhotic alcoholics susceptible to all sorts of potentially overwhelming infections. Portal hypertension is also a serious complication of the cirrhotic fibrosis. The obstruction to portal vein flow through the liver results in the development of other vein channels to accommodate the return of blood from the abdominal organs, which ordinarily flows through the portal vein. The result is the development of varices (enlarged, engorged veins) in the stomach and esophagus. These enlarged, thin-walled veins are prone to rupture, leading to one of the most serious complications of cirrhosis of the liver—bleeding varices. This constitutes an emergency and calls for immediate intervention in the form of measures to control the bleeding. A variety of therapies are available, all of which have been employed with a varying degree of success that depends on the severity of the hemorrhage and the skill and experience of the physician. Once the bleeding has been controlled, the patient should be considered for an appropriate permanent venous shunt procedure whereby venous blood bypasses the liver. Finally, total decompensation of liver cell function may cause coma and death.

The good news is that even when there is irreversible cirrhosis at the tissue level, death may not be inevitable. Survival depends mainly on two factors: luck and alcohol abstinence. Abstaining alcoholics with cirrhosis can stabilize and survive on what's left of their liver tissue without necessarily and relentlessly progressing to one of the fatal outcomes.

Risk Factors for Alcoholic Liver Disease. There are no certain answers to the question of who is likely to get alcoholic liver disease. Fatty liver is an almost universally predictable response to heavy alcohol consumption, but this by itself is seldom a serious problem. A smaller number of people develop alcoholic hepatitis and still fewer (variously estimated in different populations between 5 percent and 25 percent of alcoholics) end up with cirrhosis. Considering the large number of alcoholics in the general population, the minority who develop cirrhosis still represent large numbers; cirrhosis is one of the leading causes of all deaths.

Still, why do some alcoholics develop alcoholic hepatitis and cirrhosis, while others who drink equally heavily do not? The amount of alcohol consumption and the length of time of heavy drinking is certainly one risk factor. Gender may be another: women's livers generally are more vulnerable to the effects of alcohol than those of men, given equal alcohol exposures. Chronic viral infection, especially chronic Hepatitis C infection, has been shown to be another risk factor. Finally, there may be a genetically determined but still unclarified individual susceptibility, which may explain why some people never get cirrhosis; why some do after many years of alcoholism; and why still others get cirrhosis at a young age or after a relatively short drinking career.

Prognosis and Treatment. The issues of prognosis and treatment cannot be separated. The cornerstone of treatment is complete abstinence from alcohol. Achieving abstinence can arrest the progression of liver disease, even in established cirrhosis; continued drinking leads to deterioration and death.

One therapeutic issue relating to alcoholism is relevant to liver disease. The drug disulfiram (Antabuse) is sometimes prescribed to reinforce abstinence. Its unpleasant, sometimes severe interaction with alcohol is a deterrent against drinking. Since disulfiram (as so many other drugs) has been occasionally reported to produce liver toxicity of its own, the presence of alcoholic liver disease is sometimes regarded as a relative contraindication against prescribing disulfiram. Some clinicians believe, however, that liver toxicity caused by alcohol far outweighs any risk that may be caused by disulfiram. Another drug used to treat alcohol dependence, naltrexone (Revia, Vivitrol), can also cause liver injury when given in excessive doses. Its use in patients with active liver disease requires careful consideration by the prescribing physician. Another drug for the maintenance of abstinence, acamprosate (Campral), does not have the disadvantage of the other two agents. Its elimination is dependent on the kidney, rather than the liver, and can be used to reinforce abstinence even in individuals with mild-to-moderate liver impairment.

Other treatment techniques beyond abstinence have been proposed to aid in recovery from alcoholic liver damage. In the late 1980s, a Toronto research group reported the beneficial effect of propylthiouracil (PTU). PTU is a drug normally used for the treatment of thyroid disease, but by reducing oxygen demand in the body (including in the liver), it might help to repair the damage caused by alcohol. The early results were promising but have not been confirmed by other researchers. Other drugs, such as corticosteroids (to decrease inflammation) or colchicine (to decrease scar formation) have dubious value.

There are relatively effective treatments available for some of the complications of alcoholic liver disease that enable patients to survive and thus begin their abstinence program. Fluid accumulation in the extremities (edema) or in the abdomen (ascites) can he helped by diet modifications (salt restriction), water-removing drugs (diuretics), albumin infusion, or tapping the abdomen with a needle to withdraw fluid.

Infections can be treated with antibiotics. The brain syndrome associated with liver failure (so-called hepatic encephalopathy or, in severe cases, hepatic coma) can improve with dietary means (protein restriction) or some drugs (e.g., neomycin, lactulose). Potentially or actually bleeding esophageal varicose veins can be obliterated by sclerotherapy, a

procedure in which certain injections are delivered through a gastroscope (a tube inserted through the mouth that makes it possible to visualize the stomach). Risk of bleeding can be lessened by beta-blocking (heart-rate slowing) drugs or some surgical procedures to decrease pressure.

Finally, there is the possibility of liver transplantation. If all else fails, a successful liver transplant cures alcoholic liver disease. Apart from the general problems of donor matching and supply, some people have raised objections to offering transplantation for alcoholic liver disease on ethical grounds, claiming that the condition is self-inflicted. This is not an acceptable objection and goes against medical ethics. Well-motivated recovering alcoholics are entitled as much as anybody else to a life-saving procedure. In fact, studies have shown that the dramatic and heroic nature of this operation may be an extremely powerful motivator for future abstinence by liver recipients. Numerous successful transplants have been carried out on alcoholics.

DRUGS AND THE LIVER

Although many drugs in medicinal use may be toxic to the liver, most of the psychoactive drugs that people tend to abuse are not known to be particularly harmful. Occasional liver damage has been reported with solvent sniffing and cocaine use, but this is not a common problem. Narcotics (opioids), anti-anxiety, and other sedative drugs (such as barbiturates), marijuana, and hallucinogens do not usually cause liver injury.

There are, however, several relevant secondary issues concerning drug abuse and the liver. For one, a damaged liver (for example, from alcohol or hepatitis) results in poor tolerance of sedatives, because good liver function is necessary to eliminate sedatives properly. Impaired liver function can therefore result in an exaggerated sedative effect. Conversely, some sedatives, notably barbiturates (which were often abused in the past and sometimes still are), actually stimulate (induce) certain liver enzymes, which can result in increased elimination (i.e., decreased effect) of another therapeutically necessary drug. For example, a barbiturate user (or abuser) may have poor effect from a clotting preventative (anti-coagulant) drug that is necessary in heart disease or after a stroke. Some drugs do the opposite: they inhibit liver enzymes. For example, the anti-ulcer drug cimetidine (Tagamet), which has no psychoactive effect per se, can cause such enzyme inhibition. If a person at the same time also happens to use or abuse a sedative, the sedative can have an exaggerated effect. Generally speaking, the normal liver transforms or inactivates drugs to less active or harmless forms. A notable and important exception is acetaminophen, one of the most commonly used medications against pain and fever (e.g., the various Tylenol preparations). The liver can transform acetaminophen into a toxic metabolite that can cause a potentially lethal liver injury. Generally, this does not happen at ordinary therapeutic acetaminophen dose levels. In the case of an acetaminophen overdose, however, such severe liver toxicity can occur that a person will die within days. Most of such overdoses are, of course, suicide attempts.

Acetaminophen itself does not have any psychoactive (mind-altering) properties; thus people do not abuse it to induce euphoria. Many combination narcotic prescription painkillers, however, contain acetaminophen. People seeking narcotic *highs* from such preparations might inadvertently ingest acetaminophen in large enough quantities to subject themselves to potentially severe liver injury. The person who is overdosing with suicidal intent is more likely to be discovered and brought to quick medical attention than an unintentionally overdosing drug abuser. Unfortunately, the antidote against acetaminophen poisoning, acetylcysteine, is effective only if it is given within a few hours (less than a day) after the ingestion of the drug. By the time acetaminophen poisoning has been suspected, the opportunity for treatment with the antidote may have already passed. An additional issue with acetaminophen is strong evidence of increased risk when alcohol and acetaminophen are combined. In alcoholics, relatively low doses of acetaminophen can cause severe and potentially fatal liver damage.

Viral Hepatitis in Drug Abusers. The major cause of liver damage in those individuals who abuse drugs is not direct toxicity from the drug, but rather from the transmission of viruses from person to person through contaminated needles and syringes. The problem of viral hepatitis, then, is largely that of injecting drug users (IDUs). At least five types of disease-causing hepatitis viruses

have been identified, designated by the letters A to E. Of the five, Hepatitis A and E are not particularly associated with injecting drug abuse; but the other three are, and they will be discussed in some detail.

Hepatitis B. Hepatitis B (which used to be called serum hepatitis) is endemic to some parts of the world, such as Southeast Asia, where as many as 10 percent of the population may be infected. In the Western world, IDUs represent the greatest reservoir for Hepatitis B virus. It is transmitted through a direct blood-borne route, such as the following:

1. Contaminated needles and syringes (which drug addicts notoriously did not sterilize in the past).
2. From an infected mother across the placenta and through the umbilical cord of a developing fetus.
3. From accidental needle-stick injuries involving contaminated blood in health care workers.
4. From any blood-to-blood contact occurring during sexual intercourse. At one time blood transfusions were a common source of infection, but screening tests can now identify infected donors.

The symptoms of Hepatitis B infection vary. In its severest form, it can cause general malaise, fever, jaundice, coma, and death. The majority of patients, even with marked jaundice and fever, do not die. Many infected people do not even have an overt illness; they may not feel sick at all or may just have transient, flu-like symptoms. There may be a tender enlargement of the liver. If such people are tested in the laboratory, they have elevated liver enzymes, such as AST (also known as SGOT) and ALT (also known as SGPT), which are usually much higher than the values found in alcoholic liver disease. The bilirubin (bile pigment) level will be high if the person has yellow jaundice. The diagnosis is confirmed when serologic tests are positive for a viral particle called Hepatitis B antigen. Those who recover from the illness and clear the virus from their bodies will develop a protective antibody that will prevent them from becoming infected again. The antibody can be detected in a laboratory test.

The majority of people who get infected with Hepatitis B recover and acquire protective antibodies. A sizable minority of those who survive, however, perhaps 10 percent, will continue to carry the virus, remaining *antigen positive*. Some of these individuals will have a chronic liver inflammation that will develop into cirrhosis. The cirrhosis caused by Hepatitis B is essentially similar to alcoholic cirrhosis, with the same consequences and potential complications described above. Moreover, Hepatitis B has the potential to cause liver cancer in some of those who develop cirrhosis. Not only is Hepatitis B in such chronically infected individuals a threat to their own survival, but it is also a source of infection to others, particularly to their needle-sharing partners, to their sexual partners, and to their developing fetuses and newborn babies.

A vaccine to prevent Hepatitis B has been available in the United States since 1982; however, it was not until the introduction of a recombinant form of the vaccine in the early 1990s that universal immunization for all newborns and adolescents became feasible. While most individuals born in the 1990s and many born in the 1980s are now immunized, millions of Americans remain unvaccinated. The Advisory Committee on Immunization Practices (ACIP) recommends that all IDUs be immunized against Hepatitis B infection. Other individuals for whom immunization is strongly recommended include sexually active heterosexuals with more than one sex partner within a six-month period or those who have contracted a sexually transmitted disease; men who have sex with men; persons at occupational risk of infection (e.g., health care professionals); hemodialysis patients; household or close contacts of persons with chronic Hepatitis B viral infection; residents and staff of institutions for the developmentally disabled; persons with chronic liver disease or human immunodeficiency virus (HIV) infection; and international travelers to areas of the world where Hepatitis B is endemic.

Hepatitis C. Until about 1990, Hepatitis C was called non-A-non-B Hepatitis, because there were viral hepatitis cases that were caused by neither of the two identifiable viruses, A and B. An antibody test can now identify this virus, which is called Hepatitis C. The antibody detected is not a protective antibody, but it is similar to the AIDS (HIV) antibody in that it indicates the presence of the virus. Many cases of viral hepatitis caused by

blood transfusions in the past were due to Hepatitis C infection. The antibody test can eliminate this source of transmission, as it is used to screen the donor blood supply.

Injecting drug users, however, remain a major reservoir and source for the spread of this virus. Hepatitis C is transmitted similarly to Hepatitis B—and, for that matter, to HIV—primarily through direct blood-to-blood contact (by contaminated injection paraphernalia) and to a lesser extent, but still possibly, via sex and from mother to fetus. The primary infection very often goes unnoticed. The laboratory tests, in addition to Hepatitis C antibodies, will show elevated ALT and AST levels. Because Hepatitis C is a newly identified virus, its natural history is not yet clear. A fair amount of evidence suggests that chronic hepatitis, eventual cirrhosis, and liver cancer may be an even greater risk with Hepatitis C than it is with Hepatitis B. Some studies in the medical literature indicate that 50 to 80 percent of intravenous drug addicts may be infected with Hepatitis C.

Hepatitis D. Hepatitis D is a very unusual virus, which was originally called delta agent and later renamed Hepatitis D. It is an incomplete virus that can exist only in the presence of Hepatitis B. When the two organisms combine, the outcome is a particularly nasty, potentially lethal hepatitis, both in terms of acute mortality and chronic consequences. Discovered in Italy about 1990, in North America Hepatitis D is known to be primarily harbored by the IDU population.

PREVENTION AND TREATMENT OF VIRAL HEPATITIS

Obviously, the best prevention for injection drug users would be to stop injecting drugs. Other, often more realistic prophylactic measures—as with HIV—are the use of sterile (or at least bleached) needles and syringes, needle exchange programs, and condoms for sexual activities.

Immediately after a known or suspected exposure to Hepatitis B, the injection of an antibody preparation known as Hepatitis B immune globulin can prevent illness. A more permanent prophylaxis in high-risk populations is provided by the Hepatitis B vaccine, which gives long-term immunity in previously uninfected individuals. IDUs certainly represent one of these high-risk populations, although the widespread use of the Hepatitis B vaccine in this group raises some obvious logistic dilemmas. As of 2008, there is no passive or active immunization available for Hepatitis C.

During the first decade of the twenty-first century, a number of new agents were introduced for the treatment of chronic Hepatitis B and C infections. Hepatitis C infection can be treated with the combination of two antiviral drugs: pegylated interferon (PegIntron, Pegasys) and ribavirin (Rebetol, Copegus). Pegylated interferon must be injected once weekly and can cause severe side effects, including flu-like symptoms, fatigue, irritability and depression. Ribavirin is better tolerated but is ineffective alone and must be used in combination with the interferon. The treatment is given over a period of months; some patients are still not able to clear the virus after a year's therapy. Treatment success depends on a number of factors, including the strain of virus being treated and the patient's ability to tolerate the interferon side effects. Hepatitis B can also be treated with a form of interferon (Intron A), which is successful in eliminating the virus in about half of all patients treated. Two oral agents are also used: lamivudine (Epivir HBV) and adefovir (Hepsera). These drugs can sometimes eliminate the Hepatitis B virus; but even if they do not, when taken long term they can suppress viral replication, potentially preventing liver damage. Finally, as mentioned under alcoholic liver disease, the most radical form of therapy in the end stages is liver transplantation.

See also **Needle and Syringe Exchanges and HIV/AIDS; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Social Costs of Alcohol and Drug Abuse.**

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LIVER (METABOLIC)

Worldwide, alcohol (also called ethanol or ethyl alcohol) is one of the most commonly used mood-altering drugs. Alcohol, in different quantities for different people, is also a toxic drug: When used to excess, it taxes the body's economy, produces pathological changes in liver and other tissues, and can cause disease and death. In urban areas of the United States, just one of the complications—scarring or cirrhosis of the liver—is the fourth or fifth most frequent cause of death for people between the ages of twenty-five and sixty-five. Understanding how the sequential steps in the metabolism of alcohol correspond to specific changes in liver and other tissues promises to improve prospects that rational methods can be developed to prevent and treat alcohol abuse.

PATHOLOGY OF ALCOHOL ABUSE

Alcohol abuse affects all organs of the body (Lieber, 1992a). It atrophies many tissues, including the brain and endocrine glands. Indeed, altered hepatic (liver) metabolism plays a key role in a variety of endocrinological imbalances, such as gonadal (sex organ) dysfunctions and reproductive problems. Alcohol also exerts toxic effects on the bone marrow; it alters hematological status, causing macrocytic anemias (in which red blood cells are larger and less functional than normal), and it scars the heart and other muscles. This entry focuses mainly on the liver and gastrointestinal tract, as these are the sites where alcohol enters the body and has some of its most serious effects; this focus also provides examples of the insights and possible benefits that can be derived from the application of information from biochemistry, pathology, and molecular biology.

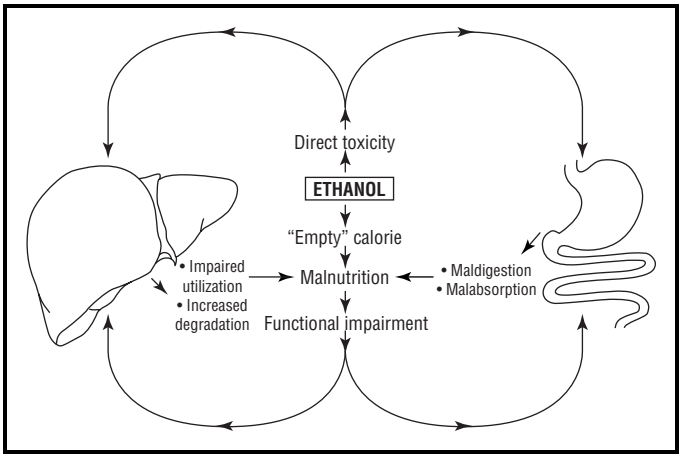

Figure 1. Interaction of direct toxicity of ethanol on liver and gut with malnutrition secondary to dietary deficiencies, maldigestion and malabsorption. (Adapted from Lieber, C. S. (1991a). *Alcohol, liver, and nutrition.* Journal of the American College of Nutrition, 10 *602–632.*) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Liver disease, one of the most devastating complications of alcoholism, was formerly attributed exclusively to the malnutrition associated with alcoholism. Indeed, nutritional deficiencies are common in the alcoholic for various reasons, some socioeconomic, but these deficiencies also occur because alcohol is a unique compound. Alcohol is a psychoactive drug; but unlike other drugs that have negligible energy value, alcohol has a high energy (calorie) content—each gram of alcohol contributes 7.1 kilocalories, which means that a cocktail or a glass of wine provides 100 to 150 kilocalories. Thus, alcoholic beverages are similar to food in energy terms; but unlike food, they are virtually devoid of vitamins, protein, and other nutrients; they provide empty calories.

As shown in Figure 1, because of its large energy load, alcohol decreases the appetite for food and displaces other nutrients in the diet, thereby promoting primary malnutrition (Lieber, 1991a). Nutrition is also impaired because alcohol affects the gastrointestinal tract. Alcohol-induced intestinal lesions, including pancreatitis (inflammation of the pancreas), are associated with maldigestion and malabsorption, causing secondary malnutrition. Moreover, malnutrition itself creates functional impairment of the gut. Finally, alcohol (ethanol or its metabolite acetaldehyde) also adversely affects nutritional status by altering the hepatic activation or

degradation of essential nutrients. Indeed, in experimental animals, malnutrition may produce a variety of liver alterations, including fatty liver and fibrosis; however, the relative contribution of malnutrition to the development of liver disease in the alcoholic cannot be clearly quantified as of 2008.

Furthermore, studies have shown that either the initial liver lesion (the fatty liver) or the ultimate stage of cirrhosis can be produced by excess alcohol, even in the absence of dietary deficiencies (Lieber & DeCarli, 1991), because ethanol (via its metabolism and/or its metabolite acetaldehyde) exerts direct hepatotoxic (toxic to the liver) effects. Thus, malnutrition plays a permissive but not a necessary role in alcohol-related somatic pathology.

METABOLISM OF ETHANOL AND SOME INTERACTIONS

Ethanol is readily absorbed from the gastrointestinal tract. Only 2 percent to 10 percent of that absorbed is eliminated through the kidneys and lungs; the rest is oxidized (metabolized) in the body, principally in the liver. Except for the stomach, extrahepatic (outside the liver) metabolism of ethanol is small. This relative organ specificity probably explains why, despite the existence of intracellular mechanisms to maintain homeostasis (equilibrium), ethanol disposal produces striking metabolic imbalances in the liver (Lieber, 1991b). These effects are aggravated by the lack of a feedback mechanism to adjust the rate of ethanol oxidation to the metabolic state of the hepatocyte (liver cell) and the inability of ethanol, unlike other major sources of calories, to be stored in the liver or to be metabolized or stored to a significant degree in peripheral tissues. As summarized here, the displacement by ethanol of the liver's normal substrates (targets of metabolism) and the metabolic disturbance produced by the oxidation of ethanol and its products explain many of the hepatic and metabolic complications of alcoholism.

A major pathway for ethanol metabolism involves alcohol dehydrogenase (ADH), an enzyme found in the cytoplasm of cells that catalyzes the conversion of ethanol to acetaldehyde. Liver ADH exists in multiple molecular forms (isozymes) that arise from various permutations of different types of subunits. Extrahepatic tissues contain isozymes of ADH with a much lower affinity for ethanol than the hepatic isozymes; as a consequence, at the levels of ethanol achieved in the blood, these extrahepatic enzymes are inactive; therefore, extrahepatic metabolism of ethanol is negligible, with the exception of gastric (in the stomach) metabolism. Because of the extraordinarily high gastric ethanol concentration after alcohol consumption, even the gastric ADH with low affinity for ethanol becomes active, and significant gastric ethanol metabolism ensues. This action decreases the bioavailability of ethanol and represents a kind of protective barrier against systemic effects, at least when ethanol is consumed in small amounts. This gastric barrier disappears after the stomach is removed (gastrectomy; Caballeria et al., 1989) and may be lost, in part, in the alcoholic, because of a decrease in gastric ADH (Di Padova el al., 1987).

Similar effects may also result from gastric ADH inhibition by some commonly used drugs. For example, aspirin and certain drugs used to treat ulcers (histamine H2-blockers; Di Padova et al., 1992) inhibit gastric ADH activity and result in increased blood levels of ethanol when alcohol is consumed in amounts equivalent to social drinking. Furthermore, women have a lower gastric ADH activity than do men (Frezza et al., 1990); as a consequence, women's blood ethanol levels are higher for a given intake, an increase that is compounded by their body composition (more fat, less water than men) and on average, a lower body weight. Their higher blood ethanol levels in turn may contribute to women's greater susceptibility to alcohol.

Alcohol dehydrogenase converts ethanol to acetaldehyde and hydrogen. Hydrogen is a form of fuel that can be burned (oxidized). Normally, the liver burns fat to produce the energy required for its own functioning; but when alcohol is present, its hydrogen displaces fat as the preferred fuel. When the liver stops burning fat and instead burns the hydrogen from the ethanol, however, fat accumulates and a fatty liver develops, which is the first stage of alcoholic liver disease (Lieber, 1992a). Once a fatty liver has developed, fat accumulation does not increase indefinitely, even though alcohol consumption may continue (Salaspuro et al., 1981). Fat deposition is offset at least in part by the secretion of fat in the form of lipoprotein, resulting in hyperlipemia (elevated amounts of fat in blood).

Hyperlipemia of a moderate degree is commonly associated with early stages of alcoholic liver injury but wanes with the progression of liver disease (Lieber & Pignon, 1989). In some individuals, marked hyperlipemia may develop, sometimes associated with Zieve's syndrome—hemolytic anemia, fatty liver, and jaundice.

This metabolic condition represents the potentiation by alcohol of an underlying abnormality in the metabolism of either lipids (essential hyperlipemia) or carbohydrates (prediabetes, pancreatitis). In addition, the degree of hyperlipemia is also influenced by the duration of alcohol intake. The capacity for a hyperlipemic response develops progressively and is accompanied by an increased activity of enzymes of the endoplasmic reticulum (within the living cells) engaged in lipoprotein production. This hyperlipemia involves all lipoprotein classes, including high-density lipoproteins (HDL), which have been said to be involved in protection against atherosclerosis and in the lesser incidence of coronary complications in moderate drinkers compared to total abstainers. However, factors other than alcohol may also contribute to this apparent protection. The ability of the liver to respond with hyperlipemia reflects the integrity of the hepatocytes; its capacity decreases with the development of more severe liver injury.

The chemical reaction associated with ethanol oxidation in the liver is known as hepatic redox, a contraction of reduction/oxidation. Elucidation of the hepatic redox reaction via the alcohol dehydrogenase pathway has furthered understanding of associated disorders in carbohydrate, purine, and protein metabolism, including hypoglycemia (low blood sugar), hyperlactacidemia (excessive levels of lactic acid in the blood), and acidosis as well as hyperuricemia (elevated uric acid levels in blood) (Lieber, 1992a). In addition to the enzyme ADH, alcohol is also oxidized in the liver by the enzyme system referred to as the microsomal ethanol-oxidizing system (MEOS), which involves a specific cytochrome P-450 (P450IIE1) (Lieber, 1987). Contrary to ADH, this pathway is inducible by chronic alcohol consumption. In rat livers (Lieber et al., 1988) and in liver biopsies of heavy drinkers (Tsutsumi et al., 1989), a five- to tenfold increase of this alcohol-inducible form was found. This induction represents one of the most striking biochemical differences between heavy drinkers and normal subjects and provides an explanation for the metabolic tolerance to ethanol—a more rapid metabolism—that develops after alcohol abuse. The induction spills over to microsomal systems that metabolize other substrates, resulting in cross-tolerance to other drugs—not only sedatives and tranquilizers but also many commonly used medications such as anticoagulants and hypoglycemic agents. Thus, heavy drinkers require an increased dosage of many commonly used medications, at least at the initial stage, prior to the development of severe liver disease. When severe liver disease develops it will offset the enzyme induction, at which time drug dosage may have to be decreased.

What complicates the treatment of heavy drinkers even further is the fact that the microsomal enzymes (especially P450IIE1) also activate many xenobiotic agents (substances from outside the body) to become highly toxic compounds. This reaction explains the increased vulnerability of heavy drinkers to the hepatotoxic effects of industrial solvents, anesthetics, analgesics (painkillers), and chemical carcinogens. The latter contribute to the increased incidence of various cancers in the alcoholic. Alcohol has a major impact on gastrointestinal cancers, with a significant increase in the incidence of neoplasms (tumors) of the oropharynx, the esophagus, the stomach, the liver, and the colon (Garro & Lieber, 1990). Alcohol also plays a role in the activation of commonly used drugs and even over-the-counter analgesics such as acetaminophen (Tylenol, also known as paracetamol) to toxic metabolites (Sato et al., 1981). Additionally, in the heavy drinker, both the breakdown and hepatic depletion of vitamin A are increased (Leo & Lieber, 1982), with adverse consequences. Also, alcohol increases the toxicity of vitamin A (Leo et al., 1982), complicating supplementation with the vitamin in the presence of alcohol abuse. Alcohol abuse additionally promotes the microsomal breakdown of testosterone and its conversion to estrogens, which, together with testicular toxicity and decreased testosterone production, results in hypoandrogenism (loss of masculinity) (Lieber, 1992a).

In addition to environmental factors, individual differences in rates of ethanol metabolism appear to be genetically controlled. The role of heredity in the development of alcoholism in humans is still under investigation as of 2008. The induction of the

previously mentioned MEOS pathway also leads to increased conversion of alcohol to acetaldehyde, a highly reactive and thus potentially toxic compound.

TOXICITY OF ACETALDEHYDE

Acetaldehyde (an intermediate metabolite of alcohol) causes injury through the formation of adducts (bonds) with proteins, resulting in antibody formation, inactivation of many key enzymes, decreased deoxyribonucleic acid (DNA) repair, and alterations in cell structures such as microtubules, mitochondria, and plasma membranes (Lieber, 1988, 1992a). Acetaldehyde also promotes synthesis of hepatic collagen, the key protein of scar tissue. Furthermore, it causes glutathione depletion, thereby worsening the toxicity mediated by free radicals, which results in lipid peroxidation and other tissue damage (Lieber, 1991b). Because of the far-reaching toxicity of this metabolite of ethanol, some of the liver cells die. Their death attracts inflammatory cells, which results in the more severe stage of alcoholic hepatitis, one of the precursors to the ultimate scarring or cirrhosis.

Once cirrhosis develops, a number of complications ensue, including obstruction of blood flow, with portal hypertension (elevated pressure in the veins leading from the intestine to the liver) and life-threatening internal bleeding from distended veins, called varices. There is also a buildup of water in the abdominal cavity, called ascites (Lieber, 1992a).

Acetaldehyde is particularly elevated if drinking occurs in pregnancy; it crosses the placenta (Karl et al., 1988) and has been incriminated in the pathogenesis of the fetal alcohol syndrome (FAS), the most common preventable cause of congenital abnormalities.

The bulk of acetaldehyde is oxidized to acetate by an acetaldehyde dehydrogenase produced by the liver mitochondria. Lack of the active form of the enzyme in some Asians explains their high blood acetaldehyde and flushing reaction after alcohol intake. Disulfiram (Antabuse, a drug used to treat alcohol intake dependence) is an inhibitor of acetaldehyde dehydrogenase. It raises the acetaldehyde levels after drinking and thereby causes flushing and several adverse effects that can be utilized in an effort to sustain abstinence in patients motivated to take the compound.

TREATMENT

Alcoholics suffer commonly from malnutrition. Therefore, nutritional deficiencies when present should be corrected, although such efforts were found to be ineffective in fully preventing liver disease due to the intrinsic toxicity of ethanol (Lieber, 1991b; Lieber & DeCarli, 1991). Although progress is being made at offsetting the direct toxicity of ethanol through chemical means (Lieber, 1992b), as of 2008 the single fully effective way of preventing somatic alcoholic injury remains control of the toxic agent ethanol through control of consumption. Complete abstinence is required in those who are genetically (or otherwise) prone to develop craving or to exhibit dependence, or those who are predisposed to develop the major somatic complication with chronic use of alcohol. For the others, moderation is recommended. What is considered *moderate* or *excessive* has been the subject of debate. One view is that on the average, moderate drinking represents no more than one drink a day in women and no more than two drinks a day in men, with a drink being 12 ounces of regular beer, 5 ounces of wine, or 1.5 ounces of distilled spirits (80 proof) (Dietary Guidelines, 2005). It is important, however, that *excess* be defined individually, taking into account not only gender, but also heredity and personal idiosyncrasies.

See also **Addiction: Concepts and Definitions; Cancer, Drugs, and Alcohol; Naltrexone; Social Costs of Alcohol and Drug Abuse.**

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MENTAL DISORDERS

The terms *comorbidity* and *dual diagnosis* describe the co-occurrence of two or more distinct psychiatric disorders. A range of psychiatric disorders, including affective disorders, anxiety disorders, and personality disorders, are often comorbid with substance use and substance use disorders (SUDs), which include alcohol and drug abuse and dependence. The association and interaction between specific SUDs and psychiatric disorders, the underlying reasons for their frequent co-occurrence, and the most effective treatments for SUD and co-occurring psychiatric diagnoses are important research areas that have been the subject of numerous studies and still require extensive future investigation.

The literature on the treatment of co-occurring psychiatric and substance use disorders is quite limited, with a particular paucity of studies evaluating non-pharmacologic interventions. The most extensively studied treatments are those for SUDs that are co-occurring with mood and anxiety symptoms and disorders. Although some studies show efficacy for specific interventions, many do not. Further, of the studies that show better outcomes for treatments that target co-occurring psychiatric symptoms, many fail to show an improvement in SUD outcomes (Nunes & Levin, 2004).

An important aspect of identifying and understanding common associations between SUDs and other psychiatric disorders involves knowing the time course of the disorders. Knowledge of which disorder is primary and which is secondary in time, or whether they developed simultaneously, provides researchers and clinicians with an improved understanding of the causation of these disorders; their general characteristics, development, and outcome; and the optimal treatment approaches. One explanation for comorbid SUD and psychiatric disorders is the *self-medication* hypothesis, in which substance use develops after the onset of the other psychiatric disorder as a means of coping with psychiatric symptoms. Another possibility

is that substance use and SUDs precede the psychiatric disorder and induce neurochemical, biological and psychological changes that increase vulnerability to other psychiatric disorders. A third possibility is that SUDs and comorbid psychiatric disorders arise from a shared vulnerability; this vulnerability could involve genetic, familial, and/or environmental risk factors and stressors. Generally the presence of an SUD increases the risk of developing other psychiatric disorders and vice versa. Additionally, psychiatric disorders are often more strongly and consistently associated with substance dependence than with substance abuse alone.

SAMPLES AND STUDY DESIGNS

General Population Samples. Between the 1980s and the early twenty-first century, four large-scale epidemiologic surveys collected data on SUDs and comorbid disorders in the general U.S. population. These surveys have all used structured interviews conducted by non-clinician interviewers. They are, however, dissimilar in other respects, such as their diagnostic criteria, instruments, sampling techniques, definition of what constitutes a *current diagnosis*, and the types of disorders and other variables they investigated.

The first of these surveys, the Epidemiologic Catchment Area Survey (ECA), was conducted at five sites and used the Diagnostic Interview Schedule to investigate prevalence and comorbidity of *DSM-III* SUDs and affective, anxiety, and psychotic disorders. The second was the National Comorbidity Survey (NCS), which used the Michigan version of the Composite International Diagnostic Interview (UM-CIDI) to collect data on SUDs, affective, anxiety, and psychotic disorders based on *DSM-III-R* criteria. The third survey, conducted in 1992, was the National Longitudinal Epidemiologic Survey (NLAES), which drew from a larger sample than the previous studies and focused on SUDs and depressive disorders; the NLAES used the Alcohol Use Disorders and Associated Disabilities Interview Schedule (AUDADIS), which gathered sufficient data for later *DSM-IV* diagnoses of SUDs and other psychiatric disorders.

The fourth survey, which is large-scale, is the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Wave 1 of the NESARC collected data on SUDs, affective, anxiety, and personality disorders, various sociodemographic variables, and family history from 43,093 respondents ages 18 and older. The NESARC achieved a response rate of 81 percent and collected data from respondents that were excluded from the NLAES, such as college students who live in group quarters; blacks, Hispanics, and young adults were oversampled. The NESARC implemented the *DSM-IV* version of the AUDADIS (AUDADIS-IV). Because of the size and scope of its sample, the NESARC is capable of providing precise and accurate information on SUD and psychiatric disorder risk by ethnic group.

Clinical Samples. Clinical studies include only patients in treatment for SUDs and/or other psychiatric disorders. Factors that influence rates of prevalence and comorbidity in clinical samples include diagnostic definitions, treatment admission policies, the study's exclusion and inclusion criteria, and sample size, which may be small. Treatment samples are susceptible to selection biases, which may result in overestimates of comorbidity and prevalence; individuals with more than one disorder are more likely to enroll in treatment. Studies, however, that draw on clinical samples may contribute to the understanding of how one disorder affects the course and outcome of another.

SUBSTANCE USE DISORDERS AND AFFECTIVE DISORDERS

Depression and Substance Use Disorders. Data from the ECA, NCS, and NLAES indicate strong associations between major depression and current and lifetime SUDs, with odds ratios (ORs) ranging from 1.9 to 7.2 depending on the survey. NESARC data on alcohol use disorders showed a significant association between major depressive disorder (MDD) and lifetime alcohol dependence (OR = 1.4), with the odds ratio adjusted for various sociodemographic characteristics and the presence of other psychiatric disorders; current (past 12-month) alcohol dependence showed a significant association with MDD when the odds ratio were adjusted for sociodemographic characteristics only (Hasin et al., 2007a). By contrast, both lifetime and current alcohol abuse were not significantly associated with MDD. In an analysis of NESARC data on current and lifetime drug use disorders, both current and lifetime drug dependence were significantly associated with MDD

(OR= 2.2 and OR 1.5, respectively) and dysthymia (OR = 2.8 and 1.7, respectively); lifetime but not current abuse showed significant associations with MDD (Compton et al., 2007). Among NESARC respondents with MDD, rates of any alcohol use disorder were 14.1 percent and 40.3 percent for 12-month and lifetime timeframes, respectively (Hasin et al., 2005); drug use disorder prevalence was 4.6 percent and 17.2 percent for 12-month and lifetime timeframes.

The strength of associations between SUDs and MDD may vary with ethnicity. In the NESARC sample, odds ratios for the association between current alcohol use disorders and MDD were significantly greater in blacks than in whites; for drug use disorders, the odds ratios were significantly greater in both blacks and Native Americans (Huang et al., 2006a). Differences may also be observed when comparing individuals with substance-induced depressive episodes and independent depressive episodes, as was done in a sample from the Collaborative Study on the Genetics of Alcoholism (COGA). Although the depressive symptoms experienced by both groups were similar, those with substance-induced depression were more likely to have greater maximum drinking levels, SUD or antisocial personality disorder diagnoses, and to be male, not white, and less educated. Compared to individuals without depression, those with substance-induced depression also reported a significantly more extensive family history of alcoholism (Schuckit et al., 2007).

Data from a study of male twins (n = 3372) suggests reciprocal causation between MDD and alcohol dependence, in which MDD increases the risk of alcohol dependence and alcohol dependence increases the risk of MDD (Lyons et al., 2006). The presence of alcohol dependence in one twin was associated with an increased risk of alcohol dependence only or combined dependence and MDD in the other twin, though not MDD only; and when one twin had MDD only, it was associated with an elevated risk of MDD only or combined MDD and alcohol dependence in the other twin, but not dependence only. In addition to a mechanism of reciprocal causation, the results could be explained by the presence of correlated genetic and environmental influences on alcohol dependence and MDD. A sibling-pair analysis identified linkage on chromosome 1 for alcoholism and depression phenotypes (Nurnberger et al., 2001). In a COGA sample, a number of single nucleotide polymorphisms (SNPs) in the CHRM2 gene on chromosome 7 were associated with alcohol dependence, depression, or a combined phenotype (Wang et al., 2004), findings that were replicated by Luo and colleagues (2005). Both SUDs and depressive disorders also have strong familial components.

Comorbid affective disorders and SUDs are often highly prevalent in clinical settings. In the Sequential Treatment Alternative to Relieve Depression (Star*D) sample, one-third of the 4,010 patients with MDD experienced concurrent SUD. In this sample, individuals with concurrent MDD and SUD were more likely to be male, younger, divorced or never married, and/or not Hispanic. They also tended to exhibit greater functional impairment than individuals without SUD comorbidity and were more likely to experience an earlier onset of depression, a larger number of depression symptoms, more frequent comorbid anxiety disorders, greater mood variation, higher rates of suicidal ideation, and poorer self-outlook (Davis et al., 2008). Few studies have investigated treatments for dual diagnosis MDD and SUD patients, though evidence suggests that concomitant depression may predict a worse outcome for SUDs, including higher relapse rates and that remission from substance dependence is linked to a decreased risk of depression. One study showed that primary care patients with comorbid SUDs and MDD who received a better standard of care for the treatment of their depression, including better quality psychotherapy and antidepressant regimens, showed similar improvement to MDD patients without comorbid SUDs and significantly lower risk of depression at a 12-month follow-up than MDD/SUD patients who did not receive improved care (Watkins et al., 2006); the improved outcome may also be attributed, in part, to the referrals to substance abuse treatment programs that the MDD/SUD patients in quality care received, which reduced their substance use levels.

Bipolar Disorder and Substance Use Disorders. Individuals experiencing manic episodes tend also to exhibit increased drinking. The use of illegal drugs, particularly stimulants, is common among individuals with bipolar disorder. In the NESARC sample, both current and lifetime drug dependence and alcohol dependence were significantly associated with bipolar I disorder (Hasin et al., 2007a; Compton et al., 2007); current and lifetime alcohol dependence and lifetime drug dependence were also

significantly associated with bipolar II disorder. Lifetime prevalence of concomitant SUDs and bipolar I was 58 percent for alcohol use disorders and 37.5 percent for drug use disorders in the NESARC sample (Grant et al., 2005).

Among patients with bipolar I and II disorders, concurrent SUDs worsened the outcome of bipolar disorder, reduced compliance to treatments, and increased the risk of suicidal behavior (Cerullo & Strakowski, 2006); some findings suggest that drug abuse may lead to an earlier onset of bipolar I disorder in families that also have a history of mania (Winokur et al., 1998). One placebo-controlled trial has suggested that for individuals with bipolar disorder and alcohol dependence, a regimen of valproate and lithium significantly reduces drinking but does not impact other psychiatric outcomes (Salloum et al., 2005).

Posttraumatic Stress Disorder (PTSD) and Substance Use Disorders. Lifetime prevalence of SUDs in general population samples of individuals with PTSD ranges from 21 to 43 percent (Jacobsen et al., 2001). In a review of clinical samples of SUDs, lifetime PTSD has ranged from 26 to 52 percent, and current PTSD from 15 to 41 percent (Schafer & Najavits, 2007). Rates of PTSD/SUD comorbidity may vary with specific substances as well. In a sample drawn from the Australian general population (Mills et al., 2006), alcohol use disorders were the most common SUDs among individuals with PTSD, with a prevalence of 24.1 percent. Among individuals with SUDs, PTSD was most prevalent among those with opioid use disorders (33.2%) and sedative use disorders (28.5%), compared to 5.4 percent of individuals with alcohol use disorders and 5.2 percent with cannabis use disorders.

Several mechanisms may explain the association between PTSD and SUDs. One is the self-medication hypothesis, which posits that individuals use substances to cope with posttraumatic symptoms. A second is the *high-risk* hypothesis, in which substance use and associated high risk behaviors increase the chances of an individual experiencing a traumatic event and subsequently developing PTSD. A third, the *susceptibility* hypothesis, asserts that the risk of PTSD increases due to the vulnerability in the brain and body brought about by heavy substance use or SUDs. Lastly, PTSD and SUDs may be affected by a third variable, such as general poor coping skills (Schafer & Najavits, 2007).

Certain environmental cues exert a particular influence on substance use in individuals with PTSD. Human laboratory studies have shown that, compared to neutral cues, exposure to trauma-related cues increases craving for substances in individuals with PTSD. PTSD/SUD patients who have recently become abstinent after SUD treatment were more likely to report substance use relapse in response to negative emotions than to substance-related cues; generally, situations involving negative emotions, conflict, high stress, and bodily discomfort are linked to greater substance use in these dual diagnosis patients.

PTSD/SUD patients generally report poorer health and functioning, increased psychiatric comorbidity, and earlier onset of substance abuse than patients presenting with either diagnosis alone. PTSD may also interfere with SUD treatment by decreasing treatment adherence and increasing the chances of relapse. Among dual diagnosis individuals, the seeking safety model—a psychotherapy that teaches coping skills in multiple domains—appears across several studies to be an effective treatment for comorbid PTSD and SUDs. More research is needed to explore effective pharmacological treatments for dual PTSD and SUD diagnoses.

Even in the absence of PTSD, substance use has been associated with exposure to traumatic events. In studies conducted among Israeli high school students, proximity to terrorist attacks was associated with greater subsequent use of alcohol and cannabis, even after depressive and posttraumatic symptoms were controlled for (Schiff et al., 2007). Following the 9/11 attacks on the World Trade Center, alcohol consumption (Wu et al., 2006; Vlahov et al., 2004) and cigarette and cannabis use (Vlahov et al., 2004) increased among New York City residents. Proximity to the 9/11 attack and past alcohol dependence also predicted higher levels of drinking after the attack in a sample of adults from northern New Jersey (Hasin et al., 2007b).

SUBSTANCE USE DISORDERS AND OTHER ANXIETY DISORDERS

Substance Use Disorders and Panic Disorders. A close relationship exists between alcohol use disorders and panic disorders (Cosci et al., 2007). The self-medication hypothesis may apply to panic disorders and alcohol use disorders and so might the

possibility that panic symptoms arise from neurochemical changes associated with heavy alcohol use, dependence, and withdrawal and to an increased sensitivity to carbon dioxide, which may increase the risk of panic symptoms. Alcohol use disorders and panic disorders may also stem from a strong familial component; family history studies have shown a relationship between alcohol use disorders and panic disorders, as in one study in which the risk of panic disorder was significantly greater (OR = 1.9) in 8,296 relatives of alcoholic probands compared to 1,654 controls (Nurnberger et al., 2004).

ECA and NCS data suggest that panic disorder increases the risk for both alcohol and drug dependence (Regier et al., 1990; Kessler et al., 1997). When the odds ratios were adjusted for various sociodemographic variables and other psychiatric disorders, lifetime alcohol dependence in the NESARC sample was significantly associated with panic disorder without agoraphobia (OR = 1.3) and lifetime drug dependence was associated with panic disorder with and without agoraphobia (OR = 2.4 and 1.6, respectively) (Hasin et al., 2007a; Compton et al., 2007). In the NESARC sample, associations between any panic disorder and alcohol use disorders were significantly stronger in Asians than in whites, blacks, and Native Americans; among Hispanics, the association was significantly stronger than in whites.

Substance Use Disorders and Other Anxiety Disorders. As with panic disorders, other anxiety disorders are commonly comorbid with SUDs. NESARC findings, with odds ratios adjusted for sociodemographic variables and other psychiatric disorders, show significant associations between current and lifetime drug dependence and generalized anxiety disorder (ORs = 2.5 and 1.6, respectively), lifetime alcohol dependence and specific phobia (OR = 1.4), and any lifetime alcohol use disorder and social phobia (OR = 1.2).

For alcohol use and anxiety disorders, comorbidity could arise in part from an interaction of anxiolytic and anxiogenic processes (Kushner et al., 2000). Drinking could provide short-term relief from anxiety but also lead to the expectation that anxiety will return once drinking is stopped; this expectation could in turn lead to more drinking and the emergence of a feed-forward cycle in which overall levels of drinking and anxiety increase. The risk of anxiety disorders and SUDs may also be transmitted through the family, as shown in family history studies in which relatives of alcoholic probands exhibit significantly higher rates of anxiety symptoms and disorders.

SUBSTANCE USE DISORDERS AND PERSONALITY DISORDERS

Borderline Personality Disorder. SUDs are highly prevalent among individuals with Borderline Personality Disorder (BPD), across community, inpatient and outpatient samples (Trull et al., 2000). Across BPD samples, rates of SUDs range from 22.7 to 86 percent. For studies of BPD and SUD comorbidity it may be difficult for patients to describe traits associated with their BPD alone, as substance use is associated with and contributes to impulsivity, interpersonal problems, and emotional dysregulation and instability. Some findings point to an association between alcohol sensitivity, alcohol use and impulsivity/disinhibition, a central trait of BPD. Impulsivity may lead to a number of risky behaviors, including the heavy use of alcohol and drugs. The development of comorbid BPD and SUDs may stem from personality traits such as impulsivity and poor emotional regulation that are central to both disorders.

Antisocial Personality Disorder. SUDs and antisocial behavior frequently co-occur. Current and lifetime alcohol dependence, drug dependence, and drug abuse are significantly associated with antisocial personality disorder in the NESARC samples (Hasin et al., 2007a; Compton et al., 2007). Twin and family studies have shown that drug abuse and dependence, alcohol dependence, childhood conduct disorder, and adult antisocial behavior share an underlying genetic liability (Kendler et al., 2003), a key reason why they so frequently co-occur. Substance dependence, childhood conduct disorder, and antisocial personality disorder appear to fall on a single underlying spectrum of externalizing psychopathology. Analyses of COGA data have provided evidence for an association between the GABRA2 gene, located on chromosome 4, and alcohol dependence; significant association has also been found between GABRA2 and drug dependence (for marijuana and other illegal drugs), childhood conduct disorder, and antisocial personality disorder (Dick, 2007). Another

COGA study tested the association between SNPs in the CHRM2 gene and a general externalizing factor comprised of alcohol and drug dependence, antisocial personality disorder, conduct disorder, and the personality traits of novelty seeking and sensation seeking; the association was tested for the factor as a whole and for the individual components. One SNP was related to alcohol dependence, another to drug dependence, and two each to novelty seeking and sensation seeking. The general factor was significantly associated with 6 SNPs, a larger number than any of its individual components; however, the single SNP related to alcohol dependence was not related to the general factor as a whole (Dick et al., 2008).

GENERAL ISSUES

Studies focusing on two types of disorders when investigating comorbidity frequently fail to control for other disorders. This pattern is especially true in cases of SUDs, affective, and anxiety disorders, which commonly co-occur. When other psychiatric disorders are controlled for, often there will be a decrease in the magnitude of the association between the two disorders studied. The understanding of treatment and functioning might also significantly improve with proper control for comorbidity, suggesting that in some dual diagnosis cases the more severe clinical presentation might result from a general burden of psychiatric comorbidity rather than a specific relationship between the two disorders studied.

More research is needed on integrated treatment for individuals with comorbid SUDs and other psychiatric disorders. Treatments tailored to only one disorder also tend to work for patients with dual diagnoses. For example, a substance use intervention will reduce substance use both in patients with SUDs only and in patients with comorbid SUDs and another psychiatric disorder. However, there are mixed findings as to whether the improvement in one disorder will carry over to the other disorder in comorbid patients (Nunes & Levin, 2004). For a large number of disorders it was unclear as of 2008 which integrated treatments would be more efficacious than treatments tailored to a single disorder. As of 2008, many studies of integrated treatments for SUD and comorbid disorder had not been replicated, perhaps due to the fact that they suffered from small sample sizes and high attrition rates. Further, these studies are not randomized or well-controlled, do not verify patient reports of symptoms, and/or do not measure key treatment outcomes and effects (Tiet & Mausbach, 2007); across studies diagnostic definitions may also be inconsistent.

Often these studies also fail to examine the interaction of the effects of medications with substance use and psychiatric symptoms. Prescription medications are also liable to be improperly used. NESARC data on non-medical prescription drug disorders show that these disorders are strongly associated with a number of Axis I and II psychiatric disorders (Huang et al., 2006b; Agrawal et al., 2006). Among mood disorders the strongest association with non-medical prescription drug use disorders is with bipolar I disorder, among anxiety disorders the strongest association is with panic disorder with agoraphobia; and among personality disorders the strongest association is with antisocial personality disorder (Huang et al., 2006b).

See also **Conduct Disorder and Drug Use; Epidemiology of Alcohol Use Disorders; Epidemiology of Drug Abuse; Research: Measuring Effects of Drugs on Mood; Risk Factors for Substance Use, Abuse, and Dependence; Social Costs of Alcohol and Drug Abuse; Structured Clinical Interview for DSM-IV (SCID).**

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NEUROLOGICAL

Alcohol and other psychotropic drugs affect the central nervous system (CNS) and its activity, thereby altering cognitive functioning. The specific substance or combination of substances consumed, the quantity in which they are used, and the duration of their use are factors influencing the effects of substances on CNS structural and functional integrity. This entry reviews the acute and chronic effects of alcohol and other psychotropic drugs on the CNS and on cognitive functioning. The studies reviewed have used a variety of methodologies, including neuropsychological tests, magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), and positron-emission tomography (PET), to assess neurocognitive alterations and attempt to link those alterations to specific structures and systems in the CNS.

ALCOHOL

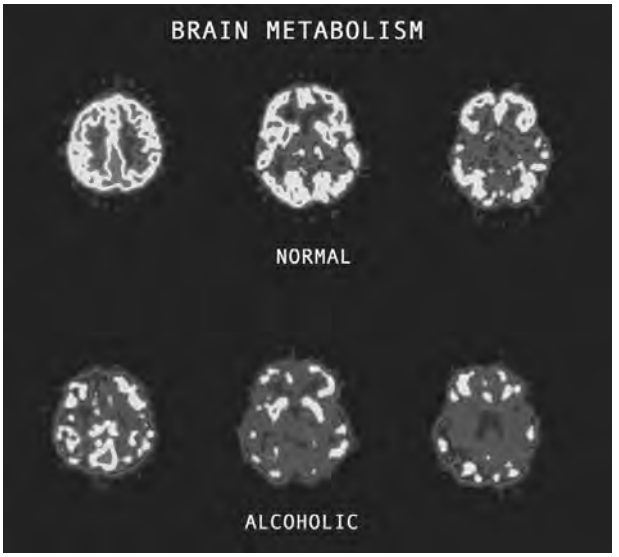
Alcohol is a CNS depressant, and acute alcohol intoxication typically results in impaired judgment, slurred speech, and uncoordinated motor movements. Other cognitive functions such as selective attention, decision-making, and hand-eye coordination may also suffer impairment during intoxication. Diminished inhibitory control, coupled with an intoxicated individual's inability to evaluate the consequences of his or her actions, can increase risk-taking, aggressive, or dangerous behaviors. Alcohol intoxication is often linked to traumatic injuries, including traumatic brain injuries. Binge drinking, in which a large quantity of alcohol is consumed within a relatively short amount of time, can lead to memory lapses and alcoholic blackouts; when experiencing a blackout, an individual cannot recall events that took place during the period of intoxication. Extremely high doses of alcohol depress consciousness, leading to sleepiness, coma, respiratory depression, and death. The effects of acute intoxication are dose dependent, although the specific doses of alcohol needed to experience these effects are influenced by factors such as body weight and tolerance.

Across studies that administer neuropsychological tests to long-term, heavy drinkers and/or individuals with alcohol use disorders, the most consistent cognitive deficits appear to be in the domains of attention, memory (including declarative memory and short-term memory), visuospatial learning and functioning, postural stability, and a set of executive functions that includes decision-making, problem-solving, working memory, and response inhibition (Crews et al., 2005; Sullivan et al., 2002; Sullivan et al., 2000). These impairments may worsen in direct proportion to the duration and frequency of drinking (Parsons, 1998; Beatty et al., 2000) or may be detectable only after a minimum of several years of heavy drinking (Eckardt et al., 1998). The impairments may also result from traumatic brain injuries suffered during intoxication and from the direct effects of alcohol itself.

Heavy and long-term drinkers suffer from neuronal damage and decreased brain volume. MRI studies

have shown that the damage and loss of volume in heavy drinkers tend to be most severe in the frontal lobes, temporal lobes, anterior hippocampus, and cerebellum (Pfeifferbaum et al., 1995; Rourke & Loberg, 1996), areas linked to executive cognitive functions, memory, and motor movements. However, cell loss is not restricted to these brain regions only and may be widespread throughout a number of cortical and subcortical areas. Autopsy studies have shown that the brains of alcoholics are smaller and weigh less than the brains of non-alcoholic controls. The brains of chronic heavy drinkers also evince enlarged sulci (the cortex's furrows and fissures) and ventricles, further evidence of volume loss; however, research on the correlation between enlarged ventricles and poorer performance on neuropsychological measures has yielded inconsistent findings (Bates et al., 2002). Alcohol has a direct toxic effect on neurons and is also linked to a loss of neurogenesis (the formation of neurons), particularly in the hippocampus, a region associated with the encoding and formation of new memories. Damage to these areas may underlie the cognitive deficits seen in heavy long-term drinkers and the increased loss of control and compulsive drinking associated with alcohol dependence. PET studies have also revealed a drop in glucose metabolism in the frontal lobes among individuals with alcohol use disorders (Johnson-Greene et al., 1997); the metabolic decrease is associated with poor performance on neuropsychological tests, particularly executive function tasks, even in the absence of cortical atrophy.

Alcohol also alters the CNS by directly interacting with neurotransmitters and modifying their activity. Alcohol enhances the activity of gamma-aminobutyric acid (GABA), the main inhibitory neurotransmitter in the CNS. Chronic alcohol use reduces the efficiency of GABA receptors, a reduction linked to an increased risk during alcohol withdrawal of excitotoxic neuronal damage which results from abnormally increased activity and transmission of excitatory neurotransmitters such as glutamate. GABA(A) receptors mediate tolerance, anxiolysis, motor coordination impairment, and several other important alcohol effects. GABRA2, a gene located on chromosome 4, encodes the alpha-2 subunit of the GABA(A) receptor. The gene has been associated with alcohol dependence (Covault et al., 2004; Edenberg et al., 2004) and with brain wave oscillations in the beta frequency range (Porjesz et al., 2002), an endophenotype related to alcohol dependence. Another neurotransmitter associated with drinking behavior is serotonin, which has also been implicated in mood regulation, sleep, and impulsive and aggressive behaviors. The serotonin transport protein (5-HTT), which takes released serotonin back up into the presynaptic neuron, controls the extracellular concentration of serotonin. Some evidence suggests that 5-HTTLPR, a promoter region polymorphism in SLC6A4, the gene encoding the 5-HTT, interacts with child abuse and maltreatment in predicting early drinking among children from low-income families (Kaufman et al., 2007). Acute alcohol intoxication has also been shown to inhibit glutamate, a neurotransmitter involved in learning and memory. It is possible that this inhibition plays a role in alcohol-related blackouts (Bates et al., 2002).



A PET scan compares a normal brain with that of alcoholic. ISM/PHOTOTAKE

There is evidence of partial recovery of neurocognitive functioning and brain mass after a period of abstinence from heavy, chronic drinking. Neuroimaging studies show decreases in ventricular size and increases in the volume of gray and white matter after abstinence (Pfefferbaum et al., 1995; O'Neill et al., 2001; Sullivan et al., 2000). There is also evidence of renewed neurogenesis in the hippocampus, as seen in the appearance of new dentate gyrus cells (Bartels et al., 2007); this neurogenesis contributes to learning, memory and the regulation of mood. However, other studies among

heavy drinkers show that decreased blood flow in the cerebellum may persist even after months of abstinence and that the cognitive abilities most vulnerable to alcohol—such as memory, problem-solving, abstraction, and selective and divided attention—may also take months or years before recovery is evident. Some evidence suggests that former heavy drinkers who are currently abstinent do not rely on the same neural systems they once used for the performance of various cognitive tasks (Pfefferbaum et al., 2001; De Rosa et al., 2004). However, these individuals may use new and more widely spread areas, resulting in decreased cognitive efficiency; an example of this is a study of verbal working memory, in which chronic drinkers used larger areas of frontal cortex than controls (Desmond et al., 2003). Cortical recovery following long-term heavy drinking may also involve a reorganization of neurocognitive processing and strategies (Crews et al., 2005).

CANNABIS

Cannabis is the most widely used illegal drug world-wide. Acute intoxication results in disruptions of attention, memory, and perceptual-motor functioning. As with alcohol, cannabis also impairs decision-making abilities and complex visual and motor functioning, so that an intoxicated individual cannot safely drive or operate heavy machinery.

Studies administering various neuropsychological tests to chronic cannabis users have shown that, compared to controls, chronic users tend to demonstrate poorer performance on tasks related to attention, memory, and executive function; cannabis users also experience a loss of self-control and behavioral inhibitions (Hall et al., 1999; Fletcher et al., 1996; Roger & Robbins, 2001). Frequency and duration of use, as well as effects of cumulative dosage, have all been associated with these cognitive impairments (Bolla et al., 2002; Solowij et al., 2002). However, a meta-analytic review of neuropsychological studies among cannabis users did not show significant impairments in various domains; the most prominent effect was a subtle memory deficit (Grant et al., 2003).

Neuroimaging studies, including those using PET and fMRI, have linked impairments in attention, verbal and working memory, and decision-making to alterations in activation, tissue volume and density, and blood flow particularly in the prefrontal cortex, basal ganglia, anterior cingulate, and hippocampus regions (Mathew et al., 1997). Heavy users also show decreased cerebellar metabolism (Volkow et al., 1996). Some research has shown reductions of up to 12 percent of the hippocampus volume and 7.1 percent of the amygdala in long-term heavy cannabis users. Dense concentrations of cannabinoid receptors are typically found in areas of the cerebral cortex, hippocampus, and basal ganglia; there are speculations that cannabinoids interfere with activity between these regions, which in part may account for the disruptions in attention and memory seen in heavy users.

Compared to non-users of cannabis, different patterns of blood flow and brain activation have been observed in chronic users when confronted with the same cognitive tasks (Lundqvist, 2005). In performing spatial working memory tasks, long-term heavy users appear to experience greater and more widespread brain activity than controls, suggesting that they have decreased cognitive efficiency and subtle widespread impairments in neurocognitive performance. In tasks of verbal recall, heavy users have shown decreased blood flow in the prefrontal cortex. Cognitive deficits may be reversible, at least in part, after a period of abstinence, though further research is required as of 2008 to determine the duration of the impairments.

OPIATES

Opiates lead to a generalized depression of cognition and intoxication may result in impaired perception, memory, learning, and reasoning, which are accompanied by changes in mood and drowsiness.

Chronic heroin use has been associated with deficits in impulse control (Pau et al., 2002; Davis et al., 2002; Lee & Pau, 2002). Heroin and other opiate users also perform poorly on reward-based decision tasks (Madden et al., 1997). Although some evidence suggests that current heroin users may show deficits in a number of cognitive domains such as attention and memory before detoxification (Guerra et al., 1987; Lee & Pau, 2002), other evidence indicates that there are no significant or long-lasting deficits in attention or cognitive tasks requiring mental flexibility (Pau et al., 2002; Davis et al., 2002). Long-term heroin users also appear to be vulnerable to lesions in the frontal and temporal lobes (Ornstein et al., 2000).

In neuroimaging scans, individuals with opiate dependence show decreased gray matter in the fusiform gyrus, prefrontal, and superior temporal cortex; there may also be a widening of the ventricles, which indicates a loss of brain volume. A reduced concentration of the neuronal marker N-acetylaspartate (NAA) and glutamate/glutamine may also be found among opiate addicts. For cognitive tasks, opiate dependent individuals have shown increased frontoparietal and cerebellar activation compared to non-user controls, indicating a decrease in cognitive efficiency. Opiate dependent individuals show particularly poor performance in tasks of spatial planning, paired association learning, and visual pattern recognition; these impairments have also been noted in currently abstinent individuals (with an average duration of abstinence of 8 years) compared to individuals with no history of opiate use (Ersche et al., 2006). However, in some tasks such as the Category Test of the Halstead Battery, which measures abstract reasoning, opiate users do not tend to show increased impairment relative to non-users, suggesting that the associated regions in the frontal lobes may be spared. By contrast, in the Tapping Test and the Tactual Performance Test for spatial memory, they do show impairment (Hill et al., 1979).

METHAMPHETAMINE AND COCAINE

Methamphetamines and cocaine act as CNS stimulants; they increase CNS arousal and psychomotor activity. The increased arousal during acute intoxication may result in a dysfunction in higher-order control processes used to monitor or inhibit ongoing behavior, such that there is a corresponding increase in errors, impulsivity, and hyperactivity. More severe consequences of even a single dose of cocaine may include seizures, strokes, and intracerebral hemorrhages.

During cognitive tasks methamphetamine users experience difficulty filtering out information irrelevant to the task; there is also evidence that they experience deficiencies in processing speed and delayed recall of information (Salo et al., 2002). Neuroimaging provides evidence that chronic methamphetamine users experience abnormal changes in frontal lobe, temporal lobe, and subcortical brain metabolism, which may result from neuronal damage to areas of the basal ganglia and frontal cortex and a decreased density of dopaminergic neurons in the putamen and caudate. Chronic methamphetamine use may lead to a decrease in dopamine transporters in the dorsolateral prefrontal cortex; an increase in these transporters after a period of abstinence has not, however, been associated with a corresponding improvement in cognitive tasks. Even after a period of abstinence lasting months, there may be lower levels of the neuronal marker NAA in the basal ganglia. Methamphetamine users also tend to show deficits in decision-making tasks that are linked to regions in the frontal cortex, particularly the ventromedial frontal cortex.

Chronic cocaine use, defined both in terms of frequency and duration, is associated with poorer performance on a number of cognitive tasks relative to non-cocaine-using controls. These tasks call on executive control, manual dexterity, psychomotor speed, verbal learning and recall, and visuospatial skills; cocaine-dependent individuals users administered the Wisconsin Card Sorting Test show poorer short-term memory as well (Rosselli & Ardila, 1996). Performance on neuropsychological tests appears to be correlated to the amount of drug used over an individual's lifetime. Cocaine use constricts cerebral blood vessels and in doing so may disrupt blood flow to various parts of the brain. There is also evidence that chronic use adversely impacts white matter maturation experienced as individuals grow older (Bartzokis et al., 2000). Reduction in brain volume and impairments on cognitive tasks may persist years after abstinence. In one study (Fein et al., 2002) a group of abstinent crack-cocaine dependent individuals showed a significant amount of reduction in prefrontal gray matter volume compared to healthy, non-user controls.

ECSTASY

MDMA use is associated with serotonergic dysfunction (Yucel et al., 2008; Montoya et al., 2002). The impairments in visual and verbal memory seen in MDMA users are linked to serotonin function and levels of 5-HIAAA (a metabolite of serotonin) in the cerebrospinal fluid, and animal studies have shown neurotoxic effects of MDMA on serotonin and dopamine neurons (Lundqvist, 2005). Chronic, repeat users also show impairments in response inhibition, attention, and coding of information to long-term

memory. Among adolescent users, abnormal functioning of the hippocampus is associated to poorer performance on tasks of working memory, an important executive function. In fMRI studies of MDMA users, abnormal activation patterns and functioning have also been observed in frontotemporal and parietal regions during working memory tests (e.g., Daumann et al., 2003). MDMA users who also consume other drugs suffer from decreased gray matter across various areas of the cortex, cerebellum, and brainstem (Cowan et al., 2003).

Neurocognitive deficits may remain for longer than six months after the period of abstinence commences. Impairments to memory and other cognitive faculties may be reversible, although the extent of recovery depends on the dosage and duration of drug use.

GENERAL ISSUES

A number of issues need to be addressed in future studies of neurocognitive impairments and neurobiological alterations in alcohol and drug users. One area of exploration is the similarities and differences in cognitive impairments when comparing different substances. Although many of the substances negatively impact similar cognitive domains, such as different aspects of memory and executive functioning, it is important to recognize the differences between substances. Doing so improves understanding of the impact of individual substances on the underlying neurobiological makeup and allows professionals to tailor more effective treatments to individuals with specific substance use disorders. For example, a comparison of heroin abusers and amphetamine abusers on measures of the Wisconsin Card Sorting Test showed that amphetamine abusers tend to perform more poorly on the measure of extra-dimensional shift but that both categories of users performed the pattern recognition measure with a similar deficits (Ornstein et al., 2000). Cognitive deficits may undermine treatment in substance using individuals even after they enter a period of abstinence; each substance may have its own negative impact on treatment strategies, which often require focus, attention, memory, and the ability to communicate, make decisions, and organize thought.

Another important issue to consider is that a number of alcohol and drug users frequently use multiple substances. A particularly frequent drug pairing, for example, is found in cannabis users who also drink. Additional research is needed on how multiple drugs interact to impact brain structure, neurotransmitter systems, and neurocognitive functioning and how the effects of polydrug use differ from the use of a single substance. One of the weaknesses in the research as of 2008 is a frequent failure to account for polydrug use in study subject populations. For example, studies have shown that drinking may be a significant confounding factor in the cognitive impairments seen in individuals with cocaine abuse (Bolla et al., 2000). Some research also suggests that cannabis may act as a confounding factor in the neuropsychological measures of ecstasy users (Croft et al., 2001).

Further investigation is needed on pre-existing neurocognitive vulnerabilities to substance use. While substance use itself exacerbates qualities such as impulsivity, lack of attention, and poor decision-making skills, there is strong evidence that these traits may also precede initial substance use. For example, individuals with attention deficit hyperactivity disorder (ADHD), conduct disorder, and/or antisocial personality disorder, as well as individuals who score high on ratings of sensation-seeking and novelty-seeking, have been shown to have a significantly higher risk of initiating substance use and developing substance use disorders than individuals without those traits or disorders (Kuperman et al., 2001; Kendler et al., 2003; Martin et al., 2002; Cloninger et al., 1995). Additionally, when substance use begins during late childhood or adolescence, when the brain has greater plasticity and is undergoing rapid developmental changes, the effects of the substance may become incorporated into brain development; for instance adolescent binge drinkers may experience more extensive damage to the frontal association cortex than later-onset binge drinkers. Substance use disorders are also highly comorbid with other psychiatric disorders, such as affective and anxiety disorders, which themselves contribute to alterations in brain structure and function and may negatively impact performance on neuropsychological tests. As of 2008 future studies were need to take better account of psychiatric comorbidity in study samples of substance users.

See also **Accidents and Injuries from Alcohol; Imaging Techniques: Visualizing the Living Brain.**

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NUTRITIONAL

Malnutrition is a common problem among abusers of alcohol and other addictive substances, contributing significantly to their deleterious effects. Nutritional problems among alcohol and substance abusers begin with inadequate or poorly selected food intake and continue with incomplete absorption or metabolism of nutrients. The effects are often insidious, and may take many years to manifest themselves. This entry not only describes the various nutritional deficits associated with substance abuse but also explains the biologic mechanisms by which they occur.

ALCOHOL

Alcoholic beverages were long used as a source of nourishment for the sick, as a means of promoting appetite, and as a treatment for pain and infection. Traditionally, wine and beer were considered foods. They were used ceremonially, including as a part of ceremonial healing for ailing (and pregnant) persons who refused or could not tolerate a solid diet. Eventually, alcoholic beverages moved from use in purely ceremonial occasions to being a reason for social occasions in some cultures, among some classes, and for some individuals. However, alcoholic beverages have a habit-forming, or addictive, element, and for some people this can become a life-threatening or fatal addiction.

The Use of Alcohol in Medicine: Recent History. In 1900, Wilbur Atwater and Francis Benedict reported on experiments they conducted at Wesleyan University, in which they attempted to define whether alcohol could actually be considered a food. They showed that alcohol is oxidized in the body and that the energy so derived can indeed be used as a fuel for metabolic purposes. Before that, in 1877, Francis E. Anstie had written his treatise *On the Uses of Wine in Health and Disease*. In fact, the long tradition of using alcoholic beverages within the medical profession persisted into the twentieth century. Sir Robert Hutchison, a noted British physician, wrote in 1905 that there was reason to believe (not that there was evidence) that alcohol increases disease resistance. Alcohol was actually used to treat serious infectious disease, such as typhus, into the late 1920s—until it was shown that patients treated with milk and beef tea had better survival rates.

The use of alcohol to treat disease was based on the belief that it would somehow overcome disability and renew strength. Other than this use, the major indication for alcohol was for analgesia (pain suppression). The basic analgesic properties of alcohol and alcoholic beverages were utilized for hundreds of years in the management of the injured and those requiring surgery. Prior to the time of anesthetics, for example, patients were offered brandy to reduce the agonizing pain of amputations. The decline and cessation of these medical uses of alcohol came about with the development of inhalation anesthetics and more efficient analgesics.

Alcohol, Obesity, and Wasting. In nonalcoholics, calories from alcohol are utilized as efficiently as calories from carbohydrates or fats, and alcohol provides more calories per gram than carbohydrates. Indeed, while carbohydrates yield 4 kilocalories per gram (kcal/gm) on combustion, when alcohol is combusted in a bomb calorimeter it yields 7.1 kcal/gm. This suggests that when alcohol is consumed in addition to a diet that maintains body weight, weight gain occurs. Fictitious characters such as Shakespeare's Sir John Falstaff suggest that obesity was already considered a characteristic of heavy drinkers in the 1600s.

The realization came about gradually that in fact chronic heavy drinking leads not to obesity but to weight loss and an inability to sustain adequate nutritional status, a condition known as "wasting." Wasted alcoholics were first portrayed by British artists such as William Hogarth (1697–1764), who were intent on showing both the social and medical evils of drinking gin—a recent import to Britain from Holland that became a fad. All ages and classes of British society indulged in the new drink. In eighteenth- and nineteenth-century England, when artists were portraying the physical deterioration associated with heavy gin drinking, it was assumed that drinking eventually led to wasting only because the drunkard was disinterested in food. This idea persisted into the twentieth century. By the 1940s, it was also well recognized that chronic alcoholics are malnourished because of an impaired utilization of nutrients.

While obesity may occur in heavy eaters who consume alcohol, it is now well-known that chronic alcoholics are undernourished. Furthermore, studies have shown that long-term, heavy consumption of

alcohol, in addition to food consumption, is not associated with the gain in body weight that would be expected from the calorie intake (Lieber, 1991). In addition, if dietary carbohydrate is replaced by alcohol, weight loss does occur (as in the so-called Drinking Man's Diet of the 1960s and 1970s). This energy deficit has been attributed to induction of the microsomal ethanol oxidizing system that metabolizes alcohol. Induction of this metabolic pathway results in increased sympathetic tone, generating heat. Charles S. Lieber, in reviewing current knowledge of the question in the early 1990s, noted that this does not explain the fact that there is little or no weight deficit when alcohol is consumed with a very low-fat diet.

Alcohol and Malnutrition. Diet-related causes of malnutrition in alcoholics include a low dietary intake of calories and nutrients. This low intake occurs because of poor appetite (which may result from the irritating effects of alcohol on the stomach lining), inebriation, and a diversion of food dollars into support of the alcohol habit. In addition, malnutrition may be caused by the impaired absorption of nutrients, poor nutrient utilization, and increased nutrient losses in body wastes. In 1940 it was suggested that alcoholism was the major cause of malnutrition in the industrialized world (Jolliffe, 1940). The impaired absorption of nutrients may result from the reduced absorptive capacity of the alcohol-damaged gut. Nutrients that are poorly absorbed by alcoholics include the B vitamins, particularly folic acid, thiamin (Vitamin B_1), and riboflavin (Vitamin B_2). Folic acid deficiency, which causes megaloblastic anemia, is particularly common in heavy drinkers.

Multiple nutritional deficiencies, including deficiencies of water- and fat-soluble vitamins, are also common in alcoholics who have pancreatic and liver disease. Chronic alcoholic pancreatitis (inflammation of the pancreas) is common in people who consume 150 grams (5.25 fl. oz) or more of alcohol per day for at least 10 years and also eat a high-fat diet. In these individuals the digestive functions of the pancreas become impaired, and therefore food is not broken down into nutrients that can be absorbed. This type of pancreatitis is a major cause of malabsorption of nutrients in alcoholics.

Alcoholic cirrhosis is a condition in which the liver cells responsible for the biotransformation of nutrients to metabolically active forms are replaced by fibrous tissue. Cirrhosis develops slowly in heavy drinkers and presents a special risk in those who consume about 35 percent or more of their total caloric intake as alcohol. Cirrhosis is the chief cause of impaired nutrient utilization in such individuals (Morgan, 1982). However, cirrhosis is caused not by a nutritional deficiency but by the toxic effects of alcohol on the liver (Lieber, 1988). Deficiencies of minerals and trace elements, particularly zinc, are common in alcoholics. Contributory causes are low intake and increased losses in the urine.

Alcohol, Nutrition, and Brain Damage. When they go on drinking sprees during which they do not eat food, alcoholics put themselves at risk for brain damage. Evidence exists for this condition only in Caucasians who are genetically predisposed, however. An acute confusional state known as Wernicke's encephalopathy may occur in those who engage in these bouts of drinking. This condition can be rapidly reversed, however, if the patient is given massive doses of intravenous thiamin within a period of 48 hours from the onset of the symptoms. If this acute condition is not treated with thiamin, a chronic state of irreversible brain damage, known as Korsakoff's syndrome, or Korsakoff's pychosis, develops, in which there is moderate-to-severe dementia (Victor et al., 1971).

Alcohol and Heart Disease. In the 1990s, evidence indicated that while moderate drinking may reduce the risk of heart disease, alcohol abuse increased the risk of heart disease. Alcohol has the effect of increasing blood (plasma) levels of high-density lipoproteins (HDL), and an elevation of these blood lipids is associated with a lower risk of heart disease. In a 1992 British study, it was shown that women who consume a moderate amount of alcohol (1–20 g/day) have lower triglyceride (fat) levels and higher HDL levels in their blood (Razay et al., 1992). This was interpreted by the authors of the study as strong evidence for supporting a lower risk of heart disease. It is important to note, however, that in this study the women who were the moderate drinkers were also slimmer than the nondrinking group, and lower body weight is also known to reduce the risk of heart disease. Since then, studies that have controlled for this and other potential confounding factors have

shown that moderate alcohol consumption does have a cardioprotective effect. Heart disease in alcoholics, in addition to resulting from the nutritional imbalance associated with chronic heavy drinking, can also result from the direct toxic effects of alcohol on the heart muscle (Brigden & Robinson, 1964).

Alcohol and Osteoporosis. As with heart disease, the effects of alcohol on bone formation can be positive or negative, depending on the demographic group studied and the amount of alcohol consumed. Data from the Framingham Heart Study, for example, suggest that consumption of at least 7 ounces of alcohol per week can improve bone mineral densities in older postmenopausal women. This effect is not fully understood, but it may be due to an augmentation of estrogen levels (Felson et al., 1995). The formation of new bone tissue in heavy drinkers, by contrast, is reduced in both men and women. This causes a marked decrease in bone mass and strength, leading to severe osteoporosis. Alcohol has a direct effect on bone formation, and there are also metabolic effects, including deleterious effects on Vitamin D metabolism, parathyroid hormone, and calcitonin (Sampson, 1997). Because inebriation is also associated with a high risk of falls, alcoholics who have osteoporosis are at particular risk to sustain hip fractures. While many of these effects are metabolic in nature and not directly linked to poor nutritional status, an inadequate intake of foods rich in calcium in favor of "empty" alcohol calories is an additional risk factor for osteoporosis in alcoholics (Bikle et al., 1985).

Methods for Assessing Nutritional Status in Alcoholics. One method used to assess caloric and nutrient intake in actively drinking alcoholics is direct observation, which is seldom feasible outside a treatment facility. Another method, which is also feasible only in the detoxification section of a rehabilitation facility, hospital, or nursing home, involves weighing food served.

When alcoholics are asked to recount what they have eaten, however, they may not report accurately. For example, when asked leading questions, they may provide answers that the question indicates are correct or ideal. They may provide the questioner with an account of a make-believe diet, or they may exaggerate the amounts of food they have eaten. These responses, which are worthless for the purpose of assessing the amount of calories consumed from food or for assessing the nutrients consumed, may be given by alcoholics who do not remember what they have eaten, or the purpose may be to please the dietitian, physician, or nurse seeking the information. Alcoholics may also exaggerate the amount they eat, reporting what has been served to them rather than what was actually consumed. (This type of over-reporting of food intake is also frequently found in people consuming other drugs that suppress the appetite.)

The presence of malnutrition is assessed in alcoholics (as well as non-alcoholics) by using anthropometric (body) measurements—including weight-for-height measurements, calculation of the body mass index (BMI, a person's body weight divided by the square of his or her height), or the circumference of the upper arm and the thickness of the fat on the back of the arm. Alcoholics show muscle wasting in the upper arms, which may suggest malnutrition even when body weight is not markedly decreased. Although alcoholics with advanced liver disease are frequently wasted, weight loss may not register in numerical terms because of fluid retention within the abdominal cavity (ascites).

Biochemical measurements are valuable for assessing the nutritional status of alcoholics. The measurement of plasma albumin levels is particularly important, for a value of less than 3.5 grams per 100 milliliters of plasma indicates that protein-energy malnutrition exists.

Nutrient Intolerance in Alcoholics with Liver Disease. Alcoholics with liver disease are very intolerant of high-protein diets. If high-protein diets are provided during periods of nutritional rehabilitation, alcoholics may develop signs of liver failure. Such alcoholics are also intolerant of Vitamin A if this vitamin is taken in amounts that exceed 10,000 international units (IU) per day. Continued intake of Vitamin A at a high daily dosage can worsen liver damage and precipitate liver failure (Roe, 1992).

Nutritional Rehabilitation of Alcoholics. The nutritional rehabilitation of alcoholics can be carried out successfully only when abstinence is enforced or

the alcoholic voluntarily stops drinking. If an alcoholic has advanced liver disease or impairment of pancreatic function such that digestion and absorption of nutrients are impaired, optimal nutritional status cannot be maintained. The goal of nutritional rehabilitation is the treatment of existing protein-energy malnutrition by increasing caloric intake from carbohydrates and the treatment of existing vitamin, mineral, and trace-element deficiencies. The appetite will return after alcohol withdrawal symptoms have abated, but the efficient absorption of vitamins may not be recovered until 10 to 14 days after drinking ceases. Intolerance of milk and other dairy foods is common during rehabilitation, because alcohol inhibits lactase, an enzyme involved in the digestion of milk sugars. Because of the resulting lactose intolerance, as well as the protein intolerance mentioned earlier, extreme caution should be exercised in diet prescription (Roe, 1979).

TOBACCO

Smoking diminishes the appetite, so that, on average, smokers have lower body weights than nonsmokers. Nevertheless, on average, smokers have greater waist-to-hip circumference ratios than nonsmokers. This suggests that smoking may have an effect on body-fat distribution. Central (torso) adiposity, reflected by this change in circumferential measurements, has been shown to increase the risk of cardiovascular disease. The cessation of smoking is usually associated with moderate weight gain, at least in part because of increased food intake (Troisi et al., 1991). Smoking is also associated with the depletion of systemic antioxidants, including vitamins A and C. The depletion of these vitamins may be partly responsible for some of the deleterious effects of smoking (Yanbaeva, 2007).

MULTIPLE SUBSTANCE ABUSE AND NUTRITION

The effects of multiple-drug use on nutrition depend on the properties and toxic characteristics of the drugs used, as well as the dose, frequency, and duration of use, as well as the time in life when the drugs are used. Narcotic drugs, such as heroin, impair appetite, so food intake is often diminished. If the drug is injected intravenously, malnutrition may be secondary to blood-borne bacterial infection or acquired immunodeficiency syndrome (AIDS). Amphetamine ("speed") is the stimulant drug that most inhibits appetite. If taken in large doses, amphetamines also prevent sleep and stimulate activity, so energy expenditure may be high and weight loss is common.

Cocaine and crack are also stimulants. They reduce appetite and may induce gastrointestinal symptoms such as nausea, which further lessens food intake (Brody et al., 1990). In general, unlike tobacco or alcohol abuse, the abuse of narcotic and stimulant drugs is not associated with the depletion of specific micronutrients. Rather, their use results in a general apathy toward food, characterized by a lack of appetite and, in many cases, a lack of interest in the quality of the food.

In a 1995 study of 140 cocaine- and heroin-addicted persons (without organic pathology) admitted to a hospital for detoxification, 92 percent weighed under the mean for the population and 30 percent weighed less than 80 percent of the mean for the population. Eighteen percent of the patients were considered to be severely malnourished. The majority (66%) of the patients were anorexic upon admission, with an average caloric intake of 978 kcal/day for females and 1265 kcal/day for males. Among an additional 18 patients admitted with both drug addiction and acute organic pathology, nutritional status was universally poor. The investigators noted that malnutrition in this addicted population was most closely related to female sex, degree of addiction, anorexia with poor caloric and fluid intake, and disturbed family and social support (Santolaria-Fernández et al., 1995).

SUBSTANCE ABUSE AND NUTRITION IN PREGNANCY

Relationships between substance abuse of pregnant women and impaired nutrition of their fetuses and newborns were summarized in a 1990 report by the U.S. Institute of Medicine, a branch of the National Academy of Sciences, titled *Nutrition during Pregnancy.*

Alcohol use during pregnancy can lead to poor birth outcomes. One condition in infants with specific defects in neuronal and cranial development is designated "fetal alcohol syndrome." Even the daily consumption of more than two glasses of wine or a daily mixed drink can lead to fetal alcohol syndrome, but this condition is most common among the offspring of mothers who are chronic heavy drinkers or binge drinkers. Alcohol use during pregnancy is also known to be associated with prenatal and postnatal

growth retardation. After birth, infants of heavy drinkers may fail to suck, either because of the presence of withdrawal symptoms or because of cleft palate (which may be part of the fetal alcohol syndrome).

Cigarette smoking during pregnancy can affect both maternal and fetal nutrition (Werler et al., 1985). Effects are due to an increased metabolic rate in smokers and to toxic effects from tobacco that impair the mother's utilization of certain nutrients, including iron, Vitamin C, folic acid, and zinc. Low-birth-weight infants are more likely to be the offspring of smokers than of nonsmokers. Scientists originally thought that this was because smokers consumed fewer calories than nonsmokers, and because the transfer of nutrients from the mother to the fetus via the placenta was reduced in smokers. While research continues to show that smoking has a negative impact on birth weight, scientists are now questioning whether this is due to poor nutrition or some other toxic effect of smoking (Matthews et al., 1999).

Cocaine and amphetamine use in pregnancy also lead to increased numbers of low-birth-weight infants. This may be caused by low food intake by the mother, for these drugs do reduce appetite. The risk of malnutrition in the newborns of women who have used cocaine during pregnancy is caused by the abnormal development of the infant's small intestine. These intestinal disorders in the infant may be extremely severe and may be associated with enterocolitis or bowel perforation, which can be fatal. If these infants survive, special methods of feeding via a vein (parenteral nutrition) are required. Although drugs other than cocaine are known to cause a constriction of blood vessels in pregnant women, only cocaine has been shown to produce these bowel disorders in infants (Telsey et al., 1988; Spinazzola et al., 1992).

See also **Alcohol: Chemistry and Pharmacology; Alcohol: History of Drinking; Complications: Liver (Clinical); Overeating and Other Excessive Behaviors.**

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ROUTE OF ADMINISTRATION

The mode of drug administration—ingestion (by mouth), nasal insufflation (snorting), inhalation (smoking), or injection (intravenous, subcutaneous, or intramuscular)—can be responsible for a number of medical complications to alcohol and other drug use. These complications are discussed as direct and indirect results of the various modes (route) of administration.

COMPLICATIONS DUE TO INGESTION

Ingestion is the way alcohol, liquid medicines, pills, and capsules are usually taken. Ingested drugs enter the gastrointestinal (GI) system, undergo some digestive processing, and enter the bloodstream through the walls of the stomach and intestines. Most medical complications from drug ingestion are a result of the corrosive and irritant effects of the drugs on the GI system. Alcohol and a variety of medicines, including aspirin, can cause intense, localized irritation to the GI mucous membranes, leading to ulceration and GI bleeding. Pharmaceutical manufacturers attempt to decrease the danger of GI irritation by adding buffers to their pills and capsules. Buffers are inert or non-active ingredients that cushion the corrosive effect of the active ingredients. However, if drug users attempt to dissolve pills intended for oral use and inject them, these buffers will often cause problems, such as abscesses or embolisms.

COMPLICATIONS DUE TO NASAL INSUFFLATION (SNORTING)

Medical complications from nasal insufflation (snorting) are usually caused by stimulant drugs, such as the amphetamines or cocaine. These drugs are breathed into the nose and absorbed into the bloodstream through the capillaries in the nasal mucous membrane. While these drugs cause a certain amount of surface irritation, the major damage is caused by their action as vasoconstrictors—they reduce the diameter of blood vessels and with chronic use can severely limit the delivery of blood through the capillaries to the inner membranes of the nose. The result of this is that tissue damaged by contact with the drugs is unable to repair itself, and progressive necrosis (tissue death) follows. With chronic cocaine use, this process can result in actual holes through the septum (the dividing tissue) between the nostrils. When tobacco is insufflated as snuff, the risk of cancer of the nasal passages is increased.

The nasal insufflation of drugs—especially heroin—can trigger asthmatic attacks serious enough to require treatment in a hospital intensive care unit (ICU). In one inner-city hospital, 56 percent of patients admitted to the ICU for severe asthma reported snorting heroin. Attacks were reported more frequently, but not exclusively, when the heroin was cut (combined) with adulterants such as Vitamin B_{12} or diphenhydramine, an antihistamine. None of the patients reported heroin as an asthma trigger following initial insufflation, suggesting that the attacks stem not from a direct irritant effect, but rather from a gradual allergic sensitization to the drug.

Complications Due to Smoking (Inhaling). The fastest delivery of large amounts of drug directly to the brain is through smoking (inhaling). Drugs taken in this way go directly to the lungs and are absorbed along with oxygen directly into the blood heading for the brain. The two terms, smoking and inhaling, as a means of drug intake, are clearly differentiated when, on the one hand, material is actually burned and the resulting smoke is taken into the lungs—as with tobacco or marijuana—or on the other hand, when fumes from volatile substances are inhaled, such as glue or gasoline. They may be confused or used interchangeably, however, when material is vaporized through heat and the vapor is inhaled—as with cocaine freebase (crack).

Smoking. Smoke from any material will act as an irritant to the lungs and bronchial system, eventually causing problems that can range from chronic bronchitis to emphysema or cancer of the mouth, throat, and/or lungs. Both tobacco and marijuana contain a number of tars and potential carcinogens (cancer-triggering substances), and both produce potentially toxic concentrations of carbon monoxide. Though it has been argued that tobacco is the worst danger because it is smoked very frequently, it has also been pointed out that the mode of using marijuana is worse—holding the smoke in the lungs for a long time. Epidemiologic studies have yet to prove conclusively that marijuana smoke causes severe lung disease or cancer, though its use has been linked to chronic bronchitis and emphysema. As a vasoconstrictor, nicotine in tobacco promotes mouth ulceration and gum disease. It can be said that people who smoke lose their teeth, while those who don't, don't. Besides its irritant effects, the smoking of tobacco may also promote respiratory disease by weakening the immune system and by paralyzing the cilia (the tiny hairlike organs) in the cells of the lungs that push out foreign matter.

Inhalation (Sniffing). The inhalation (sniffing) of volatile hydrocarbons, such as solvents, can cause death by asphyxiation or suffocation, can impair judgment, and may produce irrational, reckless behavior. Abnormalities also have occurred in liver and kidney functions, and bone-marrow damage has occurred. These may be due to hypersensitivity to the substances or chronic heavy exposure. Chromosome damage and blood abnormalities have been reported, and solvents have been cited as a cause of gastritis (inflammation of the stomach), hepatitis (inflammation of the liver), jaundice, and peptic ulcers; however, such effects are due more to the actions of the drugs than to the route of administration. Chronic users have developed slow-healing ulcers around the mouth and nose, loss of appetite, weight loss, and nutritional disorders. Irreversible brain damage has been reported, too. Many deaths attributed to solvent inhalants are caused by suffocation when users pass out with the plastic bags containing the substance still covering their noses and mouths. There is also a very real danger of death from acute solvent poisoning or aerosol inhalation. The mere provision of adequate ventilation and the avoidance of sticking one's head in a plastic bag are by no means sufficient safeguards against aerosol dangers.

Other hazards may include freezing the larynx or other parts of the airway when refrigerants are inhaled and potential spasms as these areas defrost. Blockage of the pulmonary membrane, through which oxygen is absorbed into the lungs, can also occur. Death may also result from the ingestion of toxic ingredients along with the aerosol substance. The possibility is made more likely by the fact that commercial products not produced for human consumption are not required to list their ingredients on the label. Individual substances may produce a spectrum of toxic reactions depending on their contents. These have included gastric pain, headaches, drowsiness, irritability, nausea, mucous-membrane irritation, confusion, tremors, nerve paralysis, optic-nerve damage, vomiting, lead poisoning, and anemia. The inhaling of aerosol fluorocarbons can cause sudden-sniffing death (SSD), wherein the heart is hypersensitized to the body's own hormone epinephrine (adrenaline), leading to a very erratic heartbeat, increased pulse rate, and cardiac arrest.

The inhaling of amyl, butyl, or isobutyl nitrites can cause intense headaches, an abrupt drop in blood pressure, and loss of consciousness through orthostatic hypotension (increased heart rate and palpitations), with a threat of myocardial infarction (heart attack).

COMPLICATIONS DUE TO INJECTION

The injection of drugs generally involves the use of the hypodermic needle, first invented in the early nineteenth century and used initially for the medical delivery of the opiate painkiller morphine, for the rapid control of intense pain. This combination was first used extensively for battlefield wounds during the Crimean War (1853–1856) and the American Civil War (1861–1865). As its name implies, the hypodermic needle pierces the skin—the dermis. Hypodermic injections may be subcutaneous, directly beneath the skin surface; intramuscular, into the muscle tissue; or intravenous, into a vein. (A number of injection-related medical complications are directly skin-related.)

While the hypodermic needle is the primary means of drug injection, drug addicts who do not have access to hypodermics have made use of a number of ingenious, and often very dangerous, substitutes. Nonhypodermic-needle means of injection may involve such paraphernalia as lancets or scalpels, or any small sharp blade to make an opening, and the

insertion of an eyedropper, tubing and bulb, or any means of squirting the drug into the resultant wound. In extremes, addicts have used such implements as a pencil, ballpoint or fountain pen, or the sharpened end of a spoon.

Intra-arterial Injection. Injections are never made intentionally into arteries. Accidental intra-arterial injection will produce intense pain, swelling, cyanosis (blueness), and coldness of the body extremity injected. Intra-arterial injection resulting in these symptoms is a medical emergency and, if untreated, may produce gangrene of the fingers, hands, toes, or feet and result in possible required amputation of these parts.

Transmittal of Disease through Injection. The greatest number and variety of medical complications of drug use caused by the mode of administration occur as a result of injection. Among the highest risk, and that with the most frequent fatal and disabling consequences, is the transmittal of disease through the use of non-sterile needles and the sharing of such needles.

Human Immunodeficiency Virus (HIV). Needle-using drug abusers comprise one of the primary high-risk populations for contracting human immunodeficiency virus (HIV). The primary recognized routes of transmission for HIV are (1) sexual contact through unprotected anal or vaginal intercourse—particularly if there are damaged tissues or sores present that provide direct access to the bloodstream; (2) contact with infected blood through needle sharing or through transfusions of blood or blood products; and (3) in utero or at-birth transmission from a mother to her baby. Acquired immunodeficiency syndrome (AIDS), the most severe and life-threatening result of HIV infection, involves the destruction of the infected person's immune system and the development of cancers and infections that the body can no longer fight off.

The incidence of HIV infection among needle-using drug abusers is closely related to local use traditions, habits, and the prevalence of HIV infection among other addicts. The highest incidence is in areas such as New York City, where there is a tradition of needle sharing or where *shooting galleries*—places where users can rent or share *works*—are commonly used and where there is a high prevalence of HIV among the homosexual population. Users in other geographical locations, such as San Francisco, seem to be more conservative in their social-usage patterns, and when they do share needles, tend to keep the same *shooting partners* over a longer period of time. HIV-prevention efforts in some areas have focused on needle and syringe exchange, while others, particularly where needle exchange is not legalized, have community-outreach workers teaching users how to sterilize their needles between each use with household bleach. The gist of both campaigns is that users who share their needles or who use dirty needles are at risk for contracting HIV through their drug use. Those who use sterile needles are not. Both approaches are considered stopgap, however, and are apt to be condemned as encouraging of drug abuse.

All needle-using drug abusers are considered at extremely high risk for HIV infection, and HIV screening is performed routinely at most drug-treatment centers. The virus has a long incubation period and may be present for seven or more years before active symptoms of opportunistic disease appear. Early symptoms may include: a persistent rash or lesion; unexplained weight loss; persistent night sweats or low-grade fever; persistent diarrhea or fatigue; swollen lymph glands, depression or states of mental confusion.

Hepatitis and Other Liver Disorders. Hepatitis B and Hepatitis C, often referred to as serum (fluid-related) hepatitis, are the most common medical complication of needle drug use. Like HIV, hepatitis can spread in other ways than needle use, such as sexual intercourse or other direct sharing of blood and bodily fluids. Several strains, however, can be spread by contaminated foods, particularly shellfish, or by unhygienic practices in food handling. Research in the 2000s indicates that some forms of hepatitis spread via an anal/oral progression, so it is recommended that hands are washed thoroughly after all bowel movements or any other anal-area or fecal-matter handling, as a means of prophylaxis.

Unlike AIDS, hepatitis is often not fatal if it is detected and treated at an early stage. Symptoms of all forms of hepatitis include fatigue, loss of appetite, pain in the upper abdomen, jaundice (yellow skin and a yellowish-to-chartreuse tinge to the sclerae [white of

the eye]), general itching, dark urine reaching the color of cola drinks with light-tan to cream-colored feces, and mental depression. Gamma globulin injection can provide short-term immunity to all forms of hepatitis and can reduce the symptoms of serum hepatitis if it is given during the gestation period. Treatment includes bed rest, nutritional support, and avoidance of alcohol or any other substance that may further irritate the liver. Caregivers should wear rubber gloves while handling patients. Patients with any form of hepatitis should avoid preparing food for others and use separate towels, bed linens, and eating utensils until symptoms disappear. Toilet seats and any spilled bedpan matter should be disinfected and hands should then be washed thoroughly with soap. Condoms should be used for any genital contact.

Hepatitis can cause hepatic fibrosis—development of fibrous tissue in the liver. It can also cause or exacerbate cirrhosis (scarring of the liver), although this is most often a result of chronic alcohol abuse. Symptoms of cirrhosis include jaundice (yellowish skin and eye whites), fatigue, ankle swelling, enlargement of the abdomen, and a full feeling in the right upper abdomen.

Tetanus and Malaria. According to Senay and Raynes, the first case of tetanus associated with needle-using substance abuse was reported in England in 1886. By the 1990s, between 70 and 90 percent of tetanus cases occurred to drug abusers. As a medical complication to drug injection, tetanus most often occurs from *skin-popping*, which is cutaneous injection. A majority of cases occur in women, and this is attributed to less-substantial venous development than in men and a smaller population with tetanus immunization.

Malaria (caused by the Plasmodium parasite) was first reported among drug users in the United States in 1926. It affects intravenous drug abusers and was brought to the United States by needle-sharing sailors who had been exposed to malaria in Africa. The initial outbreak in New Orleans spread to New York City in the 1930s and resulted in several hundred deaths from tertian malaria among drug abusers. A second outbreak occurred in the 1970s, as a result of malaria-infected U.S. veterans returning to the States from Vietnam.

The spread of both these diseases among needle-sharing drug abusers has been kept somewhat in check, particularly on the East Coast and in Chicago, by the inclusion of 15 to 30 percent quinine (a natural antimalarial), as filler, to stretch profits in illicit opioid drug mixtures in those areas. Quinine (an alkaloid from chinchona bark) is a protoplasmic poison that prevents the germination of the fastidious tetanus anaerobe, Clostridium tetani, under the skin and in adjacent muscle tissue. Although the quinine amount is not sufficient to eradicate malaria once it has taken hold in the body, it does help prevent the disease by killing the malarial parasites in the hypodermic syringe.

COMPLICATIONS TO HEART AND BLOOD VESSELS

Drug abuse is related to a number of heart and blood vessel medical complications. Some of these, such as alcoholic cardiomyopathy, are a direct result of the drug's toxic effects. Others are at least partially related to needle use.

Endocarditis, an infection of the tissues in the heart, usually a heart valve, is a progressive disease characterized by frequent embolization (fragments that break off from the inflamed area and travel in the bloodstream, where they can obstruct blood vessels) and severe heart-valve destruction that can be fatal if not treated. This disease can result from repeated injection of the infective agents into the blood system, usually from nonsterile needles and/or unusual methods of injection. Infective endocarditis is highly prevalent among drug abusers and should be suspected in any needle-using abuser who shows such symptoms as the following: fever of unknown origin; heart murmur; pneumonia; embolic phenomena; or blood cultures that are positive for Candida, Staphylococcus aureus, or enterococcus, or Gram-negative organisms.

MISCELLANEOUS COMPLICATIONS

Blood-vessel changes caused by necrotizing angiitis (polyarteritis—the inflammation of a number of arteries) or a swelling that leads to tissue loss have been demonstrated in intravenous amphetamine abusers, resulting in cerebrovascular occlusion (blockage in brain blood vessels) and intracranial hemorrhage or stroke.

Problems in the lungs often develop from inert materials that are included as cutting agents or as buffers and binding agents in drugs that come in

pill form but are liquified and injected. These substances do not dissolve, so their particles may become lodged in the lungs, causing chronic pulmonary fibrosis and foreign-body granulomas. These same buffers and binding agents may also become lodged in various capillary systems, including the tiny blood vessels in the eye.

Finally, injection-induced infections reaching the skeleton can be responsible for such bone diseases as septic arthritis and osteomyelitis. Gangrene can develop from cutting off circulation to the extremities and may necessitate amputation or be fatal.

See also **Inhalants: Extent of Use and Complications; Needle and Syringe Exchanges and HIV/AIDS.**

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COMPULSIONS. Historically, compulsions have been described as difficult to resist behaviors, regardless of the motivation. In psychiatry, the term has been used classically to describe repetitive behaviors that are performed with the goal of reducing or preventing anxiety or distress. These uncomfortable feelings have historically been referred to as "ego-dystonic." These behaviors contrast with ones motivated by the seeking of pleasure or gratification, behaviors that have been termed hedonic or "ego-syntonic." Within this context, the term "compulsion" has been applied in particular to obsessive-compulsive disorder (OCD). In OCD, compulsive behaviors are considered unwanted or distressing, and these behaviors contrast with pleasurable or hedonic ones seen in other disorders; for example, sensation- or euphoria-seeking aspects of drug addiction. In the early twenty-first century, a greater appreciation of the alterations in motivation underlying behaviors in addiction influenced the conceptualization of compulsive behaviors in addiction. Compulsions may be conceptualized as behaviors that are performed in the absence of reinforcement. As such, drug-seeking and drug-taking behaviors in drug addiction typically become more habitual or compulsive over time. Investigations of habit formation in preclinical models implicate an important role for the brain region called the dorsal striatum, and investigations of drug dependent individuals also implicate this brain region. These and other data support the notion that as behaviors move from being impulsive to compulsive in nature, there is progressive involvement of dorsal as compared to ventral portions of the striatum in the decision-making processes governing engagement in motivated behaviors.

See also **Addiction: Concepts and Definitions.**

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COMPUTERIZED DIAGNOSTIC INTERVIEW SCHEDULE FOR DSM-IV (C DIS-IV). Developed in the late 1970s for use in the first epidemiological multisite study of the prevalence and incidence of psychiatric disorders in the United States, the Diagnostic Interview Schedule (DIS) continues to hold a prominent place in the psychiatric assessment armamentarium. Now administered in a computerized format, it has been updated to reflect changes in the *DSM*. This highly structured psychiatric interview carefully operationalizes the fourth edition (*DSM-IV*) criteria into specific questions, so when administered by an interviewer, it may be used to create diagnoses according to the *DSM-IV*. The C DIS-IV has maintained most of the unique properties of the original DIS, including the hallmark infrastructure known as the PFC (Probe Flow Chart), as well as age of onset of criteria and demographic, social, and psychiatric risk factors. The computerized version expands on the original version with the addition of impairment, remission, ages of onset, and offset of risk factors. The C DIS-IV, with skip instructions built in, minimizes administration errors, making it ideal for both clinicians and trained nonclinicians.

The PFC elicits information used to determine whether a symptom is clinically significant. Only if it meets the threshold for clinical significance is the symptom probed further to explore potential causality. The PFC classifies the endorsed symptom as always attributable to medication, drugs, or alcohol; physical conditions or injuries; or possibly psychiatric in nature. For example, in the depression module, it is important to know whether the loss of appetite was ever due to a physical illness or injury, or to medication, drugs, or alcohol. If it was due to hypothyroidism and only experienced with this condition, a special code signifies physical illness or injury as the cause of the symptom. For disorders that are conditional on an exposure, such as pathological gambling, post-traumatic stress disorder (PTSD), or substance use disorders, the PFC is not necessary.

The substance use disorder module of the C DIS-IV is a comprehensive assessment of consequences of alcohol use, tobacco products, and other substances, including marijuana, stimulants, sedatives, cocaine, heroin, other opiates, hallucinogens, phencyclidine (PCP), and inhalants. Only users who meet a threshold of having used the substance more than five times in their lifetime will continue to answer questions about that substance. The route of administration of a substance is elicited, as is age of onset and offset for each drug used. Specifically, each abuse and dependence criterion is operationalized independently; quantity-frequency data for each drug are also collected. For each criterion, the number of questions created varies. Further, unlike some other diagnostic assessments, the C DIS-IV does not make a generic diagnosis of "drug abuse and/or dependence." Instead, it makes individual abuse/dependence diagnoses. The problem with the former is that there are numerous types of drugs to assess independently (such as opiates, cocaine and other stimulants, sedatives, and cannabis), and when they are lumped together, individual criteria become blurred. Also, unlike other assessments, the C DIS-IV does not use abuse questions to screen for dependence.

The complexity of the C DIS-IV can be appreciated by simply observing the number of questions used to make a diagnosis; each criterion is not necessarily assessed by only one question. For example, the alcohol module includes 32 questions for abuse and dependence; alcohol abuse is assessed with 7 questions. Nicotine dependence requires 35 questions. The drug modules all follow a similar pattern, but the specific withdrawal syndrome varies, depending on the substance. Although a withdrawal syndrome is not required for some drugs, it is assessed, for surveillance purposes. In addition to alcohol and drug use disorders, the C DIS-IV yields data needed to diagnose somatization/pain, specific phobia/social phobia/agoraphobia/panic, generalized anxiety disorder, post-traumatic stress disorder, depression/dysthymia, mania/hypomania, schizophrenia/schizophreniform/schizoaffective, obsessive-compulsive disorder, anorexia nervosa/bulimia, attention deficit disorder, separation anxiety, oppositional disorder, conduct disorder, antisocial personality, pathological gambling, and dementia.

The DIS algorithms have been extensively tested (Robins & Cottler, 2004). The C DIS-IV encompasses all the essentials of good diagnostic interviews: It accurately represents the diagnostic criterion; it captures the ill, while not incorrectly asking the unaffected; it does not double-count symptoms; it is educationally and culturally acceptable; it does not

depend on medical record review; and it has standardized questions. It is an excellent choice for investigators conducting comorbidity research (i.e., on the co-occurrence of disorders), as well as nosological research (i.e., on the classification of disorders).

See also **Addiction: Concepts and Definitions; Diagnosis of Substance Use Disorders: Diagnostic Criteria; Diagnostic and Statistical Manual (DSM); Models of Alcoholism and Drug Abuse.**

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CONDITIONED TOLERANCE.

Tolerance refers to the diminishment or the loss of a drug effect over the course of repeated administrations. Some researchers have postulated that an important factor in the development of tolerance is Pavlovian conditioning of drug-compensatory responses. The administration of a drug may be viewed as a Pavlovian conditioning trial. The stimuli present at the time of drug administration are the conditional stimulus (CS), while the effect produced by the drug is the unconditional stimulus (UCS). Many drug effects involve disruption of the homeostatic level of physiological systems (e.g., alcohol lowers body temperature), and these disruptions elicit compensatory responses that tend to restore functioning to normal levels. The compensatory, restorative response to a drug effect is the unconditional response (UCR). Repeated administrations of a drug in the context of the same set of stimuli can result in the usual pre-drug cues coming to elicit as a conditional response (CR) the compensatory, restorative response. The conditional drug-compensatory CR would tend to reduce the drug effect when the drug is administered with the usual pre-drug cues—thus accounting for tolerance, or at least some aspects of tolerance.

One test of the Pavlovian conditioning model of tolerance is whether conditional drug-compensatory responses are elicited by pre-drug cues. In one experiment with rats (Crowell, Hinson, & Siegel, 1981), injections of alcohol in the context of one set of stimuli were alternated with injections of saline solution in the context of a different set of stimuli for several days. Each day, the rats' body temperatures were measured. Alcohol lowered body temperatures the first time it was given, but this effect diminished over the course of the repeated alcohol administrations—that is, tolerance developed to the hypothermic effect of alcohol. To determine if a drug-compensatory CR was elicited by the usual pre-drug cues, the rats were given a placebo CR test. In a placebo CR test, saline solution is administered instead of the drug. The placebo CR test was given to some rats under conditions where they were expecting alcohol; that is, saline was administered with the usual pre-drug cues. For the remaining rats, the placebo CR test was given under conditions where there should have been no expectancy of alcohol; that is, saline was administered with cues that had previously signaled only saline. Rats given saline with the usual pre-drug cues had elevated body temperatures, while rats given saline without the usual pre-drug cues showed little temperature change. Thus, it was possible to directly observe the drug-compensatory CR, in this case hyperthermia opposed to the hypothermic effect of alcohol. Other experiments similar to the one just described have found drug-compensatory CRs following the development of tolerance to various effects of opiates, barbiturates, and benzodiazepines (Siegel, 1983).

Conditioned responses occur only when the conditional stimulus is presented. If drug-compensatory CRs contribute to tolerance, then tolerance should only be evident in the presence of the usual pre-drug cues that are the CS. This expectation was tested in the experiment by Crowell, Hinson, and Siegel (1981), involving tolerance to the hypothermic effect of alcohol. After all rats had developed tolerance to the hypothermic effect of alcohol, a test was given in which some rats received alcohol with the usual pre-drug cues, while other rats received alcohol when the usual pre-drug cues were not present. Although all rats had displayed tolerance prior to the test, only those rats given alcohol in the presence of the usual

pre-drug cues (i.e., with the CS) showed tolerance during the test. The explanation of this "situational specificity" of tolerance is that when alcohol is given with the usual pre-drug cues, the drug-compensatory CR occurs and reduces the drug effect—but when alcohol is given without the usual pre-drug cues, the drug-compensatory CR does not occur and the drug effect is not reduced. Other research has demonstrated situational specificity with regard to tolerance to opiates, barbiturates, and benzodiazepines (for a complete review see Siegel, 1983).

In order to eliminate a CR, it is necessary to present the CS not followed by the UCS, a procedure termed *extinction*. Research indicates that the loss of tolerance occurs as a result of extinction of drug-compensatory CRs. Again referring to the experiment of Crowell, Hinson, and Siegel (1981), rats were given alcohol in the presence of a consistent set of cues until tolerance developed. Then, all drug injections were stopped for several days. During this period some animals were given extinction trials, in which the usual pre-drug cues were presented but only saline was injected. The other animals did not receive extinction trials and were left undisturbed during this time. Subsequently, all animals were given a test in which the drug was given with the usual pre-drug cues. The animals that had received extinction trials were no longer tolerant, whereas animals that had not been given extinction trials retained their tolerance. Similar results—in which tolerance is retained unless extinction trials are given—occur for tolerance to opiates, barbiturates, and benzodiazepines (Siegel, 1983).

The drug-compensatory CRs that contribute to tolerance may also be involved in withdrawal-like symptoms that occur in detoxified drug addicts. Detoxified addicts often report experiencing withdrawal-like symptoms when they return to places where they formerly used drugs, although they are now drug free. The places where the addict formerly used drugs act as CSs and still elicit drug-compensatory CRs; even when the addict is drug free, the drug-compensatory CRs achieve expression. Thus, it is postulated that the drug-compensatory CRs elicited by the usual pre-drug cues in the drug-free post-addict result in a withdrawal-like syndrome (Hinson & Siegel, 1980). This conditional post-detoxification withdrawal syndrome may motivate the post-addict to resume drug taking (to alleviate the symptoms).

See also **Addiction: Concepts and Definitions; Risk Factors for Substance Use, Abuse, and Dependence: Learning; Tolerance and Physical Dependence; Wikler's Conditioning Theory of Drug Addiction.**

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CONDUCT DISORDER AND DRUG USE.

In the American Psychiatric Association classification system for diagnosing mental disorder (*DSM-IV*), conduct disorder (CD) is defined as "a repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated" (1994, p. 85). CD is socially disruptive and more serious in its consequences than typical childhood mischief. The duration of the behavior, its severity, and the kinds of actions involved distinguish CD from general misbehavior. In the general population of individuals under age eighteen, it occurs in 2 percent to 9 percent of females and 6 percent to 16 percent of males. Emerging evidence as of 2008 suggests, however, that the gender gap is narrowing. CD is the most common behavioral problem seen in child psychiatric settings in North America and is present in about 75 percent of emotionally disturbed youth.

DIAGNOSIS

The behaviors that characterize this disorder include: 1) aggressive conduct causing or threatening to cause physical harm to other people or animals (e.g., often

bullies, threatens, or intimidates others), 2) non-aggressive conduct causing property loss or damage (e.g., has deliberately destroyed others' property), 3) deceitfulness or theft (e.g., has broken into someone else's house, building, or car), and 4) serious violation of rules (e.g., is often truant from school, beginning before age thirteen years). Criteria for a CD diagnosis are: 1) three or more symptoms in the past twelve months, with at least one symptom present in the past six months; 2) disturbance in behavior that causes clinically significant impairment in social, academic, or occupational functioning; and 3) criteria are not met for antisocial personality disorder if the individual is age eighteen years or older.

CD is one of the most valid and reliably diagnosed psychiatric disturbances. The problem behavior is trans-situational, being manifested in the home, at school, and in daily social functioning. Often, youths with CD are suspicious of others, and, consequently, they misinterpret the intentions and actions of others. By adolescence, aggression may become so severe that violent assault, rape, and homicide are committed. Precocious sexual behavior and sexual misbehavior, especially among females, are also common. Denial and minimization generally occur when the youngsters are confronted about their behavior. Typically, feelings of guilt are not experienced.

Other, less severe, types of behavior disorders are also known. The most common that resemble CD are adjustment disorder with disturbances of conduct, childhood (or adolescent) antisocial behavior, and oppositional defiant disorder. Children may manifest different combinations of CD symptoms and exhibit CD symptoms at different points of development. Substantial differences in the behavioral manifestations of CD have prompted efforts to develop subtypes. The most well known subtypes are socialized versus unsocialized, aggressive versus non-aggressive, overt versus covert, and childhood-onset versus adolescent-onset.

One variant of CD, the solitary aggressive type, characterizes approximately 50 percent of incarcerated youths; they are usually socioeconomically disadvantaged and typically come from dysfunctional families. Moral development is arrested, cognitive abilities are low, and behavior is often dangerous both to themselves and others. This CD variant should not be confused with adaptive delinquency, in which the behavior is an attempt to adjust to the manifold disadvantages of inner-city living.

NATURAL HISTORY

Other psychiatric disorders frequently occur in conjunction with CD. The most prevalent comorbid (coexisting) psychiatric disorder is attention-deficit/hyperactivity disorder. By adolescence, there is also significant comorbidity with substance use disorders and depressive disorders.

The age of onset is earlier and the behavior problems are more severe among children with comorbid CD and attention-deficit/hyperactivity disorder than in children with either disorder alone. Children with both disorders are also at greater risk for developing criminal behavior and substance abuse by adolescence or young adulthood.

The co-occurrence of CD and substance use disorders has been observed frequently. It is estimated that as many as 50 percent of serious offenders are substance abusers. In these cases, CD usually precedes the onset of substance abuse. There is some evidence that substance use disorders and CD are the overt expressions of a common underlying predisposition. Drug use during adolescence, by virtue of its pattern of illegal behavior plus association with non-normative peers, increases the risk for violent assault as well as for getting arrested and convicted for drug possession or distribution.

Among the childhood psychiatric disorders, CD is the most likely to remain stable. One study found that 54 percent of boys with a childhood diagnosis of CD were diagnosed with antisocial personality disorder in early adulthood. Persistence of conduct problems into adulthood is most likely if the behavior problems are serious, are generalized across multiple environments or situations, have an early age of onset, and lead the person into the criminal-justice system.

ETIOLOGY

The etiology of CD is considered multifactorial. Risk factors believed to contribute to its development include difficult temperament and a family history of antisocial personality disorder and/or alcohol dependence. Mild central nervous system abnormalities have been found in children with a history of violent behavior, and these are thought to contribute

to the children's impulsivity. Neurologic injuries (e.g., secondary to head trauma) and neurodevelopmental disability (e.g., dyslexia) can exacerbate the expression of CD. Adoption, family, and twin studies implicate a genetic predisposition for the development of antisocial behavior. Several studies also indicate that there are common genetic influences between CD and ADHD, oppositional defiant disorder, and substance use disorders. However, a genetic propensity does not invariably ensure this adverse outcome. Some studies suggest that the interaction between genes and the environment may be important in the etiology of CD. Potential environmental risk factors for CD include poor parenting skills and family dysfunction (e.g., abusive, neglectful, and absent parents). Physically abusive and alcoholic parents frequently have had CD in their own childhoods. Socioeconomic factors (e.g., poverty, participation in street gangs) also influence the development of CD.

TREATMENT

Treatment of CD in children and adolescents can include family therapy, parent management training, behavioral and cognitive therapies, residential treatment programs, and, less frequently, pharmacotherapy. The most promising approaches as of 2008 include parent management training, which trains parents to reinforce prosocial behavior rather than aggressive behavior. Studies using random assignment show that parent management training is effective in improving parenting skills and reducing aggressive behavior in children.

See also **Adolescents and Drug Use; Crime and Drugs; Families and Drug Use; Intimate Partner Violence and Alcohol/Substance Use; Risk Factors for Substance Use, Abuse, and Dependence.**

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CONTROLLED SUBSTANCES ACT OF 1970. Until 1970, psychoactive drugs were regulated at the federal level by a patchwork of statutes enacted since the turn of the century. These statutes were shaped by an evolving conception of congressional power under the U.S. Constitution. The first federal law on the subject was the Pure Food and Drug Act of 1906, which required the labeling of substances such as patent medicines if they included designated narcotics (e.g., opiates and cocaine) and were shipped in interstate commerce. In 1909, Congress banned the importation of smoking opium. Then in 1914, in the Harrison Narcotics Act, Congress deployed its taxing power as a device for prohibiting the distribution and use of narcotics for nonmedical purposes. (The taxing power was used because U.S. Supreme Court decisions implied that Congress would not be permitted to use its power to regulate interstate commerce in banning "local" activities, such as the production and distribution of narcotics.) The scheme established by the Harrison Act required the registration and payment of an occupational tax by all persons who imported, produced, or distributed narcotics; it imposed a tax on each transaction; and it made it a crime to engage in a transaction without paying the tax. Mere possession of narcotics without a prescription was presumptive evidence of a violation of the act. The Marihuana Tax Act of 1937 utilized the same model.

In 1965, Congress prohibited the manufacture and distribution of "dangerous drugs" (stimulants, depressants, and hallucinogens) for nonmedical purposes. By this time, Congress's constitutional authority to enact such legislation under the commerce clause was no longer in doubt. (In 1968, Congress made simple possession of the drugs a misdemeanor.) An all-important feature of the 1965 "dangerous drug" legislation was its delegation of authority to the secretary of Health, Education and Welfare (HEW) to control previously uncontrolled drugs if they had a "potential for abuse" due to their depressant, stimulant, or hallucinogenic properties. (In 1968, this scheduling authority was transferred to the U.S. attorney general.)

All this legislation was replaced by a comprehensive regulatory structure in the 1970 Controlled Substances Act (CSA). Under the new statutory scheme, all previously controlled substances were classified—in five schedules—according to their potential for abuse and accepted medical utility; an administrative process was then established for scheduling new substances, building on the model of the 1965 act. Schedule I lists drugs that have no traditional recognized medical use, such as heroin, LSD, and cannabis (marijuana). Schedule II lists the drugs with medical uses that have the greatest potential for abuse and dependence, such as morphine and cocaine. The remaining schedules use a sliding scale that balances each drug's abuse potential and its legitimate medical uses.

Different degrees of control are applied to manufacturers, distributors, and prescribers—depending on the schedule in which the drug has been placed. The regulatory structure of the Controlled Substances Act is predicated on the assumption that tighter controls on legitimate transactions will prevent diversion of these substances and will thereby reduce the availability of these substances for nonmedical use.

The drafting of the Controlled Substances Act reflected a continuing controversy regarding the locus of administrative authority for scheduling new drugs and for rescheduling previously controlled drugs. Under the bill passed by the Senate, this responsibility would have rested with the U.S. attorney general, who was required only to "request the advice" of the secretary of HEW (now Health and Human Services, HHS) and of a scientific advisory committee; the attorney general was not required to follow this advice although the various criteria in the act require primarily scientific and medical judgments. The Senate rejected an amendment that would have made the recommendations of the "advisor" binding on the attorney general. Under the bill passed in the House of Representatives, however, the secretary's decision declining to schedule a new drug was binding on the attorney general, and the secretary's recommendation concerning rescheduling was binding as to its medical and scientific aspects. The House version prevailed in the 1970 law as it was finally adopted.

After enactment of the federal Controlled Substances Act, the National Conference of Commissioners on Uniform State Laws promulgated a Uniform Controlled Substances Act, which was modeled after the federal act. (Earlier state laws were modeled on the 1934 Uniform Narcotic Drug Act, which had also been promulgated by the National Conference.) Every state has enacted the Uniform Controlled Substances Act.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Controls: Scheduled Drugs/Drug Schedules, U.S; Legal Regulation of Drugs and Alcohol.**

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CONTROLS: SCHEDULED DRUGS/ DRUG SCHEDULES, U.S.

The Comprehensive Drug Abuse Prevention and Control Act of 1970, commonly known as the Controlled Substance Act (CSA) establishes the procedures that must be followed by drug manufacturers, researchers, physicians, pharmacists, and others involved in the legal manufacturing, distributing, prescribing, and dispensing of controlled drugs. These procedures provide accountability for a drug from its initial production through distribution to the patient to reduce widespread diversion of controlled drugs from legitimate medical or scientific use.

DRUG CONTROL AND SCHEDULING CRITERIA

Several factors are considered before a drug is controlled under this act. These factors include the potential for abuse (i.e., history, magnitude, duration, and significance), risk to public health, and potential of physical or psychological dependence. Drugs controlled under this act are divided into five Schedules (I–V) according to their potential for abuse, ability to produce dependence, and medical utility. Drugs in Schedule I have a high potential for abuse and/or dependence with no accepted medical use, or they lack demonstrated clinical safety. Those in Schedules II–V have a high potential for abuse or an ability to produce dependence but also have an accepted medical use. (However, some substances that have no accepted medical use but are precursors to clinically useful substances may also be found in Schedules II–V. For example, thebaine, found naturally in opium, has no medical use but it is a substance used in the manufacture of codeine and a series of potent opioid compounds as well as opioid antagonists.) The potential for abuse and the ability to produce dependence is the greatest for Schedule I and II drugs and progressively less for Schedule III, IV, and V (see Table 1).

The amount of controlled drug in a product can also determine the schedule in which it is placed. For example, amphetamine, methamphetamine, and codeine, as pure substances, are placed in Schedule II; however, these same drugs in limited quantities and in combination with a noncontrolled drug are placed in Schedules III and V. Drugs in Schedule V

DEA schedule	Abuse potential	Examples of drugs covered	Some of the effects	Medical use
I	highest	heroin, LSD, hashish, marijuana, methaqualone	unpredictable effects, severe psychological or physical dependence, or death	no accepted use: some are legal for limited research use only
II	high	morphine, PCP, cocaine, methadone, methamphetamine	may lead to severe psychological or physical dependence	accepted use with restrictions
III	medium	codeine with aspirin or Tylenol®, some barbiturates, anabolic steroids	may lead to moderate or low physical dependence or high psychological dependence	accepted use
IV	low	Darvon®, Talwin®, Equanil® Valium®, Xanax®	may lead to limited physical or psychological dependence	accepted use
V	lowest	over-the-counter or prescription cough medicines with codeine	may lead to limited physical or psychological dependence	accepted use

Table 1. Drugs are scheduled under federal law according to their effects, medical use, and potential for abuse. (Adapted from *Drugs of Abuse* (2005), Drug Enforcement Administration, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

	Potential for:		Medical use
Schedule	Abuse	Dependence	& safety
I	+ + + +	+ + + +	No
II	+ + + +	+ + + +	Yes
III	+ + +	+ + +	Yes
IV	+ +	+ +	Yes
V	+	+	Yes

Table 2. Criteria for U.S. drug scheduling. (Adapted from *Drugs of Abuse* (2005), Drug Enforcement Administration, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

generally contain limited quantities of certain narcotic drugs used for cough and antidiarrheal purposes and can only be distributed or dispensed for medical purposes.

LISTS OF SCHEDULED DRUGS

Drugs controlled under the CSA are listed by schedule and drug class in Table 2 (Schedules I and II) and Table 3 (Schedules III, IV, and V). A listing of controlled chemical derivatives, immediate precursors (chemical that precedes the active drug), and chemicals essential for making a controlled drug, along with drugs exempt from control can be found in the most current edition of the *Controlled Substances Handbook*. Some brand names for drugs in Schedules II–V are not included in the tables, but can be found in the latest edition of the *Controlled Substances Handbook*.

PRESCRIBING AND DISPENSING CONTROLLED DRUGS

Medical practitioners have to follow specific rules for each schedule when prescribing or dispensing controlled drugs. Drugs in Schedule I can only be obtained, prescribed, and dispensed to an individual after special approval is obtained from the Food and Drug Administration (FDA). Drugs in Schedule II cannot be refilled or dispensed without a written prescription from a practitioner, except in an emergency. When they are dispensed in an emergency, a written prescription must be obtained within 72 hours. Drugs in Schedule III and in Schedule IV may not be dispensed without a written or an oral prescription. Prescriptions for these drugs may not be filled or refilled more than six months after their issue date or refilled more than five times unless authorized by a licensed practitioner. Drugs in Schedule V can be refilled, with a practitioner's authorization, without a limitation on number of refills or amount of time. Certain Schedule V drugs may be purchased directly from a pharmacist, in limited quantities, without a prescription. The purchaser must be at least 18 years of age and furnish appropriate identification, and these transactions must be recorded by the dispensing pharmacist.

When drugs in Schedule II, III, and IV are dispensed, a warning label stating, "Caution: Federal law prohibits the transfer of this drug to any person other than the patient for whom it was prescribed," must be affixed to the dispensing container. The warning label regarding transfer does not apply to Schedule V drugs.

Schedule–I

Opiates		Opium derivatives	Hallucinogens	Depressants	Stimulants
Acetyl-alpha-methylfentanyl	Hydroxypethidine	Acetorphine	Alpha-ethyltryptamine	Mecloqualone	Aminorex Cathinone
Acetylmethadol	Ketobemidone	Acetyldihydrocodeine	4-bromo-2.5-DMA	Methaqualone	Fenethylline
Allylprodine	Levomoramide	Benzylmorphine	Alpha-desmethyl DOB		Metheathinone
Alphameprodine	Levophenacylmorphan	Codeine methylbromide	2.5-DMA		(±) cis-4-methylaminorex
Alphamethadol	3-methylfentanyl	Codeine-N-Oxide	DOET		N-ethylamphetamine
Alpha-methylfentanyl	3-methylthiofentanyl	Cyprenorphine	PMA		N.N-dimethyl-amphetamine
Alpha-methylthiofentanyl	Morpheridine	Desomorphine	5-methoxy-3,4-methylene-dioxyamphetamine		
Benzethidine	MPPP	Dihydromorphine	MMDA		
Betacetylmethadol	Noracymethadol	Drotebanol	DOM, STP		
Beta-hydroxyfentanyl	Norlevorphanol	Etorphine (except HCl salt)	MDA		
Beta-hydroxy-3-methylfentanyl	Normethadone	Heroin	MDMA		
Betameprodine	Norpipanone	Hydromorphinol	MDEA		
Betamethadol	Para-fluorofentanyl	Methyldesorphine	N-hydroxy MDA		
Betaprodine	PEPAP	Methyldihydromorphine	3,4,5-trimethoxy amphetamine		
Clonitazene	Phenadoxone	Morphine methylbromide	Bufotenine		
Dextromocamide	Phenampromide	Morphine methylsulfonate	DET		
Diampromide	Phenomorphan	Morphine-N-Oxide	DMT		
Diethylthiambutene	Phenoperidine	Myrophine	Ibogaine		
Difenoxin	Piritramide	Nicocodeine	LSD		
Dimenoxadol	Proheptazine	Nicomorphine	Marijuana		
Dimepheptanol	Properidine	Normorphine	Mescaline		
Dimethylthiambutene	Propiram	Pholcodine	N-ethyl-3-piperidyl benzilate		
Dioxaphetyl butyrate	Raccmoramide	Thebacon	N-methyl-3-piperidyl benzilate		
Dipipanone	Thiofentanyl		Peyote		
Ethylmethylthiambatene	Tilidine		Pheneyelidine analogs PCE, PCPy, TCP, TCPy		
Etonitazene	Trimeperidine		Psilocybin		
Etoxeridine			Psilocyn		
Furethidine			Tetrahydrocannabinols		

Table 3. List of controlled drugs, Schedule I. (Source: Drug Scheduling, Drug Enforcement Administration, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

REGISTRATION, ORDERING, QUOTAS, AND RECORDS

Each individual or institution engaged in manufacturing, distributing, or dispensing any controlled drug must be authorized by and register annually with federal and state drug-enforcement agencies, unless specifically exempted. A unique registration number is assigned to each individual or institution registered under the act. A separate registration is required for practitioners who dispense narcotic drugs to individuals for the purpose of addiction treatment (such as Methadone and LAAM [l-Alpha-Acetylmethadol] for opioid detoxification or maintenance).

All orders for Schedule I and II drugs must be made using a special narcotic order form. Proof of registration is required when ordering Schedule III–V drugs. Annual production quotas are established for drugs in Schedule I and Schedule II. Everyone registered to handle controlled drugs must maintain records, conduct inventories, and file periodic reports specific to their business or professional activity.

The Controlled Substances Act of 1970 also created the requirement for manufacturers and distributors to report their controlled substances transactions to the Attorney General. The Attorney General delegates this authority to the Drug Enforcement Administration (DEA). ARCOS (Automation of Reports and Consolidated Orders System) is an automated, comprehensive drug-reporting system that monitors the flow of DEA-controlled substances from their point of manufacture through commercial distribution channels to point of sale or distribution at the dispensing/retail level. ARCOS tracks transactions involving all Schedules I and II materials, Schedule III narcotic and gama-hydroxybutyric acid (GHB) materials, and selected Schedule III and IV psychotropic drugs (manufacturers only). ARCOS summarizes these transactions into reports that give federal and state investigators information that can be used to identify the diversion of controlled substances into illicit channels of distribution.

Schedule–II

Opiates	Opium & derivatives	Hallucinogens	Depressants	Stimulants	Others
Alfentanil	Raw opium	Nabilone	Amobarbital	Amphetamine	Opium poppy
Alphaprodine	Opium extracts		Glutethimide	Methamphetamine	Poppy straw
Anileridine	Opium fluid extract		Pentobarbital	Phenmetrazine	Coca leaves
Bezitramide	Powdered opium		Phencyclidine	Methylphenidate	Immediate precursors to:
Carfentanil	Granulated opium		Secobarbital		Amphetamine
Dextroprophene, bulk	Tincture of opium				Methamphetamine
Dihydrocodeine	Codeine				Phencyclidine
Diphenoxylate	Ethylmorphine				
Fentanyl	Etorphine hydrochloride				
Isomethadone	Hydrocodone				
Levo-alphacetylmethadol	Hydromorphone				
Levomethorphan	Metopon				
Levorphanol	Morphine				
Meperidine Intermediate-A	Oxycodone				
Meperidine Intermediate-B	Oxymorphone				
Meperidine Intermediate-C	Thebaine				
Metazocine					
Methadone					
Methadone-Intermediate					
Moramide-Intermediate					
Pethidine					
Phenazocine					
Piminodine					
Racemethorphan					
Racemorphan					
Remifentanil					
Sufentanil					

Table 4. List of controlled drugs, Schedule II. (Source: Drug Scheduling, Drug Enforcement Administration, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Schedule–III

Narcotics	Depressants	Stimulants	Others
Limited quantities of:	Mixtures of	Limited mixtures	Dronabinol in sesame oil
Codeine	Amobarbital	of Schedule II	in soft gelatin capsule
Dihydrocodeinone,	Secobarbital	amphetamines	Nalorphine
Dihydrocodeine,	Pentobarbital	Benzphetamine	All anabolic steroids
Ethylmorphine,	Derivatives of	Chlorphentermine	
Hydrocodone,	barbituric acid	Clortermine	
Opium, and	Aprobarbital	Phendimetrazine	
Morphine	Butabarbital		
in combination	Butalbital		
with nonnarcotics	Chlorhexadol		
Buprenorphine	Ketamine		
	Lysergic acid		
	Lysergic acid amide		
	Methyprylon		
	Sulfondiethylmethane		
	Sulfonethylmethane		
	Sulfonmethane		
	Talbutal		
	Thiopental		
	Tiletamine		
	Vinbarbital		
	Zolazepam		

Table 5. List of controlled drugs, Schedule III. (Source: Drug Scheduling, Drug Enforcement Administration, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Schedule–IV				
Narcotics	**Depressants**		**Stimulants**	**Others**
Limited quantity of difenoxin in combination with atropine sulfate	Alprazolam	Loprasolam	Cathine	Butorphanol
	Barbital	Lorazepam	Dexfenfluramine	Fenfluramine
	Bromazepam	Lormetazepam	Diethylpropion	Pentazocine
Dextropropoxyphere	Camazepam	Mebutamate	Fencamfamin	
	Chloral betaine	Medazepam	Fenproporex	
	Chloral hydrate	Meprobamate	Mazindol	
	Chlordiazepoxide	Methohexital	Mefenorex	
	Clobazam	Methylphenobarbital	Modafinil	
	Clonazepam	Midazolam	Pemoline	
	Clorazepate	Nimetazepam	Phentermine	
	Clotiazepam	Nitrazepam	Pipradrol	
	Cloxazolam	Nordiazepam	Sibutramine	
	Delorazepam	Oxazepam	SPA	
	Diazepam	Oxazolam		
	Dichloralphenazone	Paraldehyde		
	Estazolam	Petrichloral		
	Ethchlorvynol	Phenobarbital		
	Ethinamate	Pinazepam		
	Ethyl loflazepate	Prazepam		
	Fludiazepam	Quazepam		
	Flunitrazepam	Temazepam		
	Flurazepam	Tetrazepam		
	Halazepam	Triazolam		
	Haloxazolam	Zaleplon		
	Ketazolam	Zolpidem		

Table 6. List of controlled drugs, Schedule IV. (Source: Drug Scheduling, Drug Enforcement Administration, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Schedule–V	
Narcotics	**Stimulants**
Buprenorphine	Pyrovalcrone
Limited quantities (less than Schedules III & IV) of: Codeine, Dihydrocodeine, Ethylmorphine, Dipehnoxylate, Opium, and Difenoxin in combination with nonnarcotics	

Table 7. List of controlled drugs, Schedule V. (Source: Drug Scheduling, Drug Enforcement Administration, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

SPECIAL ISSUES

The development of designer drugs has raised many concerns about policing drugs of abuse. Underground chemists who develop designer drugs seek to achieve two results: the creation of marketable drugs that mimic the effects of restricted drugs of abuse and the creation of drugs that are not specifically listed as controlled substances by the Drug Enforcement Administration. The most popular designer drug of the late 1990s was MDMA (methylenedioxymethamphetamine), popularly known as Ecstasy. Despite efforts to evade federal drug laws, the designers of these drugs eventually see them added to the CSA. For example, MDMA was placed on Schedule I on an emergency basis in 1985 because of its neurotoxic effects and abuse potential. In 2007 the synthetic drug fentanyl, a synthetic opiate that is 30 to 50 times more powerful than heroin, had become a popular drug; it too was placed on Schedule I.

The abuse of prescription drugs for nonmedical purposes is the second largest form of illegal drug abuse in the United States. The federal government estimates that in 2007 approximately 6.4 million people use controlled-substance prescription drugs for nonmedical purposes, with 4.7 million misusing pain relievers. Policing prescription drugs has become more difficult with the advent of online pharmacies. Active drug cases involving the Internet increased by 25 percent in 2006, rising from 194 to 242 cases (*National Drug Control Strategy: 2007 Annual Report*, p. 31.)

State and local laws either parallel the federal regulations as described by the CSA or impose additional restrictions. Individuals registered to

handle controlled drugs must abide by the law (state or federal) that is most stringent in governing their business or professional activity. Examples of where state law may be more stringent than federal law include the requirement for Triplicate Prescription forms or the placing of a drug in a higher schedule.

See also **Addiction: Concepts and Definitions; Legal Regulation of Drugs and Alcohol.**

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COPING AND DRUG USE. Coping is the strategy used to manage stress. This process consists of two facets: *Coping style* refers to the tactics used to attenuate ongoing stress or to avoid anticipated stress. *Coping competence* refers to the cognitive, emotional, and behavioral resources deployed to manage stress.

Adaptive coping buffers the risk of developing stress-related medical illnesses and psychological disorder. An exercise routine is one example of adaptive coping because it reduces stress and improves mental and physical fitness. Maladaptive coping abates stress but at the cost of potential future adverse consequences. Because of the ubiquity of drugs that have abuse potential, substance consumption is a maladaptive coping strategy. Habitual use may lead to addiction, organ-system injury and disease, psychiatric disorders, legal problems, and social maladjustment.

Many chemicals contained naturally in plants and animals, and in modern times synthesized, are consumed to potentiate well-being in healthy individuals (e.g., vitamins, herbs, minerals, fish oil). In addition, an enormous number of chemicals are used to treat disease. From this ever-expanding pharmacopeia, a subset of chemicals acts on the neuroanatomical substrate subserving the experience of reward by affecting the release of dopamine. Accordingly, drug consumption results in the experience of pleasure (positive reinforcement) and relief from discomfort (negative reinforcement). Drugs are consumed as a coping strategy to reduce discomfort; however, both positive and negative reinforcement can occur together as, for example, during so-called happy hour when alcohol dampens stress at the end of the workday while enhancing pleasure through convivial social interaction.

Repetitive consumption results in adaptation to the drug by the brain. This process, termed *tolerance*, leads to the progressive need for increasingly higher doses to alleviate stress. Thus, as tolerance increases, drug use as a coping strategy is motivated by both the desire to reduce stress and the desire to avoid the symptoms of withdrawal.

The likelihood of using drugs as a coping strategy depends on three sets of factors: 1) characteristics of the individual; 2) number, severity, and chronicity of stressors; and, 3) availability, cost, and legal sanctions determining accessibility and desirability of compounds having addictive potential.

Many individual characteristics, albeit no specific personality type, predispose to habitual substance use. Within the population of substance users, individuals who have a constellation of characteristics indicative of stress susceptibility are, however, prone to using abusable drugs as a coping strategy. These characteristics include but are not limited to anxiety, panic reaction, phobia, and depression.

Stress is the necessary condition required to be present to promote drug use as a coping strategy. The quality of relationship with parents and peers, capacity to perform adequately and adjust to

school, and concern about physical appearance are common stressors in adolescents. Stress related to work, dissatisfaction with the intimate partner, and psychiatric disturbance frequently trigger substance use during middle adulthood. As aging progresses, declining health (including chronic pain and insomnia), depression following death of family members and friends, boredom from loss of routine following retirement, and social isolation are stressors that frequently result in psychiatric disturbance and are managed by prescription medications that have addictive potential or other compounds, especially alcohol.

Stimulants and depressants are used to manage stress. Caffeine, the most widely used psychoactive drug, boosts mood and elevates energy. Nicotine is commonly used to cope with stress. Both drugs are stimulants, indicating that pharmacokinetic and pharmacodynamic properties, along with social learning, beliefs, and attitudes contribute to drug use as a coping strategy. Alcohol, a depressant, is used to cope with a variety of stressors and accordingly is consumed for its perceived properties as an aphrodisiac, analgesic, sedative, and hypnotic.

Because stress is only one of many reasons for substance use, the presence of this association needs to be determined on a case-by-case basis. Stress can be ascertained by querying the individual about the motivation for consuming drugs. A response pointing to a desire to manage an aversive physical or emotional condition or a threatening social situation reveals that the substance is used as a coping strategy. In formal evaluation, the revised Drug Use Screening Inventory (Tarter, 1990) is an efficient method of evaluating severity of substance use in relation to psychiatric disorder, behavior patterns, health status, family system, work, and psychosocial adjustment. Obtaining information about coping style and competence can be objectively evaluated using the Ways of Coping Scale (Lazarus & Folkman, 1984). Once it is established that the person consumes drugs to cope with stress, a treatment plan can be designed to inculcate healthier strategies. Notably, prognosis is improved by enhancing coping competence in alcoholics (Getter et al., 1992) and a treatment protocol has been developed for this population (Kadden et al., 1992). Good coping skills have been shown to be predictive of abstinence from drugs in youths (Anderson et al., 2007) and adults (Hser, 2007). Thus, when substance use is a coping strategy, prognosis is enhanced by inculcating more adaptive methods to manage stress.

See also **Relapse; Treatment, Behavioral Approaches to: Cognitive Therapy.**

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CRACK. *Crack*, sometimes called *crack cocaine,* is the smokable form of cocaine. It is made by adding a base—either ammonia or, more typically, baking soda and water—to cocaine hydrochloride. The white powder called cocaine is the hydrochloride form, which is water-soluble and can be injected. It cannot be smoked, however, because it is destroyed at high temperatures. Thus, in order to be smoked, cocaine must be converted to the base state. Once the proper mixture is made, it is heated to remove the hydrochloride, resulting in a cake-like solid substance that can be smoked. This form of cocaine is generally available in small quantities, making it inexpensive and readily available for purchase "on the street." It is called "crack" because of the cracks that form in the solid mass as it dries—and because of the noise it makes when smoked.

Although crack can be smoked in tobacco or marijuana cigarettes, it is generally smoked in a special crack pipe. In its simplest form, this is a glass tube with a hole at the top of one end and a hole at the other end through which the smoke is inhaled. Most commercially available crack pipes have a small bowl at the end. The crack pellet is placed on fine wire-mesh screens that cover the hole, and a flame is applied directly to the pellet. Soda bottles, small liquor bottles, and other similar implements are all used to manufacture homemade crack pipes. What all crack pipes have in common is the fine mesh screen, which prevents the crack from being lost as it melts. A temperature of approximately 200°F (93°C) is the most efficient in providing the largest amount of cocaine to the user, as higher temperatures destroy more of the cocaine.

Smoking cocaine began with the use of "freebase" cocaine, which is prepared by its users from cocaine hydrochloride. Soon after this form of cocaine achieved its popularity in the 1980s, single doses of cocaine already prepared for smoking and known as crack became available through the illicit drug market. Unlike the process for forming freebase cocaine, the crack manufacturing process does not rid the cocaine of its adulterants. This manufactured form of smokable cocaine soon became readily available and was so convenient to use, and smoking cocaine became a popular route of administration. The levels of cocaine in the blood peak rapidly when it is smoked, because of efficient respiratory absorption, and this method yields effects (e.g., peak effects, duration of effect, half-life) comparable to the intravenous route of administration. The smoker of cocaine, however, can get the effects within about 10 seconds. This leads to a cocaine "rush" and substantial levels of cocaine in the blood. This can be done repeatedly by smoking, which is a more socially acceptable route of administration than injection and does not require the paraphernalia associated with hardcore illicit drug use (e.g., syringes, needles).

The more rapid the onset of the drug effect, the more likely it is that the drug will be abused. Thus, although the overall effects of smoking crack are no different than the effects of taking cocaine by any other route, the ready availability of small amounts of the drug for purchase and the ease with which the drug can be taken, combined with its toxicity, make this an extremely dangerous substance.

From a financial perspective, crack is more desirable for both the buyer and the seller. A gram of cocaine hydrochloride costs approximately $50 to $100. This gram can be turned into 10 to 25 crack pellets, each selling for $3 to $50. Prices vary, however, as does the purity of the crack sold. Lower prices may mean lower purity and less effect for the buyer. Still, a gram of cocaine can generate a substantial profit for the seller and make single dose units available to anyone with only a few dollars to spend.

See also **Coca Paste; Freebasing; Pharmacokinetics: General; Street Value.**

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CRAVING. *Craving* is generally defined as a state of desire, longing, or urge for a drug that is responsible for ongoing drug-use behavior, as well as relapse, among drug-dependent individuals. Craving has also been used to describe desire for non-drug related substances or activities, such as food, sex, and gambling. During periods of abstinence, drug-dependent individuals often complain of intense craving for their drug. Systems for diagnosing addictive disorders include persistent desire or craving for a drug as a major symptom of drug dependence, and many pharmacological and behavioral treatments for drug addiction focus on craving reduction as a way to reduce drug-use behavior.

The belief that an addict's inability to control drug use is caused by craving was a prominent feature of descriptions of addictive disorders provided by many nineteenth-century and early twentieth-century writers. The use of craving as a key

mechanism in theories of addiction peaked in the 1950s, supported largely by E. M. Jellinek (1890–1963) in his writings on the causes of alcoholism. Jellinek contended that sober alcoholics who consumed a small amount of alcohol would experience overwhelming craving that would compel them to continue to drink. Many clinicians and addiction researchers adopted the proposal that craving and loss of control over drinking were equivalent concepts. Equally popular was the position, also supported by Jellinek, that craving was a direct sign of drug withdrawal. Withdrawal-based craving was often described as physical craving, distinguishing it from a more psychological form of craving that led to relapse during long periods of abstinence after withdrawal had subsided. The craving concept was sufficiently controversial that a committee of alcoholism experts (World Health Organization Expert Committees on Mental Health and Alcohol, 1955) recommended that the term *craving* not be used to describe various aspects of drinking behavior seen in alcoholics.

The use of craving as a key process in theories of addiction decreased during the 1960s and early 1970s as a result of several factors. During this period, many studies showed that alcoholics did not necessarily engage in loss of control drinking when they drank small doses of alcohol. The failure to confirm Jellinek's conceptualization of alcoholic drinking cast doubt on the idea that *craving* was synonymous with *loss of control* over drug intake. Furthermore, withdrawal models of craving could not account for the common observation that many addicts experienced craving and relapsed long after their withdrawal had disappeared. Finally, addiction research was increasingly dominated by behavioral approaches that focused on the influence of environmental variables in the control of drug taking and avoided the use of subjective concepts, such as craving.

Even though many addiction researchers questioned the value of craving as an explanatory concept, it persisted as an important clinical issue, as many addicts complained that craving was a major barrier to their attempts to stop using drugs. Craving continued to be cited as a major symptom of drug dependence in formal diagnostic systems, and the notion that craving was responsible for compulsive drug use remained at the core of several popular conceptualizations of drug addiction. Scientific interest in the role of craving in addictive disorders reemerged in the middle 1970s as a result of two developments. First, behavioral theories of addiction were increasingly influenced by social-cognitive models of behavior that were more sympathetic to hypothetical entities such as craving. Second, animal research on the contribution of learning processes to drug tolerance and drug withdrawal provided support for the hypothesis that learned withdrawal effects might produce craving and relapse in abstinent addicts.

THEORIES OF CRAVING

Although in the early twenty-first century there is considerable disagreement across theories regarding the processes that supposedly control craving, nearly all models describe craving as a fundamentally subjective state. With few exceptions, modern theories of craving also assume that craving is a necessary, but probably not sufficient, condition for drug taking among addicts. These theories suppose that addicts are driven to use drugs because of their craving, and craving is generally described as the principal cause of relapse in addicts trying to remain abstinent. Most comprehensive models of craving invoke some sort of learning or cognitive process in their descriptions of the mechanisms controlling craving, and these models make little distinction between physical and psychological forms of drug craving.

Many modern theories suggest that craving may be merely a part of drug withdrawal. For example, the diagnostic system published by the American Psychiatric Association in 1987 (*Diagnostic and Statistical Manual of Mental Disorders*, 3rd ed. rev.) listed craving as one of the symptoms of withdrawal for nicotine and opioids. Other approaches assume that cravings are distinct from withdrawal but represent an addict's anticipation of, and desire for, relief from withdrawal. To explain the presence of craving following long periods of abstinence, it has been posited that learning processes are responsible for the maintenance of withdrawal effects. For example, Wikler's conditioning model of drug withdrawal hypothesizes that situations reliably paired with episodes of drug withdrawal become conditioned stimuli that can later produce conditioned withdrawal responses (Wikler, 1948). This learned-withdrawal reaction will trigger drug craving, which, in turn, may lead to relapse. A similar theory is based

on the suggestion that drug-tolerance processes can become conditioned to environmental stimuli. Some have hypothesized that conditioned drug-tolerance effects will produce withdrawal-like reactions that, as in Wikler's theory, should promote craving and relapse to drug use (Poulos, Hinson, & Siegel, 1981).

Another perspective on craving is that it is strongly associated with the positively reinforcing, or stimulating, effects of drugs. For example, Marlatt (1985) suggested that craving is a subjective state produced by the expectation that use of a drug will produce euphoria, excitation, or stimulation. Similarly, Wise (1988) proposed that craving represents memories of the pleasurable or positively reinforcing effects of drugs. There are also multiprocess models, in which expectancies of positive reinforcement and anticipation of withdrawal relief, as well as other factors, including mood states and access to drugs, generate craving (Baker, Morse, & Sherman, 1987).

The early twenty-first century saw a surge of cognitive accounts of craving. In general, cognitive accounts have increasingly emphasized the role of implicit processes as playing an important motivational influence on drug taking (Wiers & Stacy, 2006). One influential cognitive theory suggests that drug use may operate independently of craving (Tiffany, 1990). According to this theory, an addict's drug-use behavior becomes highly automatic due to a long history of repeated practice. Over time, drug use may be easily triggered by certain cues, difficult to stop once triggered, and carried out effortlessly with little awareness. Addicts attempting to withdraw from drug use will experience craving as they try to stop these automatized actions from going through to completion.

Other models have proposed specific neural underpinnings for craving. For instance, the incentive-sensitization view, which distinguishes drug liking from drug wanting, associates the latter with sensitized neural circuits related to the nucleus accumbens (Robinson & Berridge, 1993). This sensitization results in excessive incentive salience being attributed to drug-associated cues.

MEASURES OF CRAVING

Craving is generally measured through three types of behaviors: self-reports of craving, drug-use behavior, and physiological responding. Most often, addicts are simply asked to rate or describe their level of craving for a drug. Questionnaires have been developed that ask addicts to rate a variety of issues related to craving. These questionnaires are considerably more reliable than a single rating of craving and show that an addict's description of craving may have multiple dimensions. The most common measure of tobacco craving is the Questionnaire of Smoking Urges (Tiffany & Drobes, 1991), and the Obsessive-Compulsive Drinking Scale (Anton, Moak, & Latham, 1995) is the most widely used measure related to alcohol craving. Measures of drug-use behavior have also been used to assess drug craving, which is entirely consistent with the assumption that craving is responsible for drug use in addicts. Finally, as several theories posit that craving should be represented by particular patterns of physiological changes, physiological measures, primarily those controlled by the autonomic nervous system, have been included in several studies as an index of craving. These measures have included changes in heart rate, sweat gland activity, and salivation. In general, withdrawal-based theories predict that the physiology of craving should look like the physiology of drug withdrawal, and models that emphasize positive reinforcement would associate drug desire with physiology characteristic of the excitatory effects of drugs. A number of neuroimaging techniques (fMRI, PET) have attempted to address the neural underpinnings of craving. As of 2008, though, research had not clearly identified which neural systems are associated with craving, though it appeared that areas related to reward processing (e.g., ventral striatum, orbitofrontal cortex, amygdala) are likely involved.

RESEARCH ON CRAVING

Naturalistic and laboratory studies have been used to investigate drug craving. Naturalistic studies examine changes in addicts' descriptions of craving as they are attempting to stop using drugs. These studies generally have shown that cravings are especially strong in the first several weeks of abstinence, but decline over time as addicts stay off drugs. They also reveal that craving rarely remains at a constant level throughout the day, but grows stronger or weaker depending on the situations the addict encounters. These situations tend to be strongly associated with previous use of drugs, such

as meeting drug-using friends or going to locations where the addict used drugs in the past.

Laboratory studies attempt to manipulate craving by presenting addicts with stimuli or cues that have been associated with their previous drug use. For example, a heroin addict may watch a videotape of someone injecting heroin or smokers may be asked to imagine a situation in which they would want to smoke. These cue-reactivity studies allow the measurement of self-reports of craving, drug-use behavior, and physiological reactions under controlled conditions. Results from these studies indicate that abstinence from drugs, drug-related stimuli, and negative moods can increase craving.

Findings from naturalistic and laboratory studies have presented a challenge to the dominant assumption that craving is directly responsible for drug use in addicts (Kassel & Shiffman, 1992; Tiffany, 1990). For example, there is only a weak correlation between addicts' reported levels of craving and their level of drug consumption within most cue-reactivity studies. Correlations between self-reported craving and physiological reactions also tend to be weak. Other studies reveal that, although addicts frequently complain that cravings are a major difficulty, few addicts who relapse say that they experienced craving just before their relapse episode. However, when addicts are asked about their craving in general, or over a longer period of time, these ratings tend to better predict relapse. Overall, the exact function of craving in drug dependence remains controversial.

See also **Addiction: Concepts and Definitions; Conditioned Tolerance; Research, Animal Model: An Overview; Risk Factors for Substance Use, Abuse, and Dependence: Learning.**

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CREATIVITY AND DRUGS. Accounts of alcohol and drug use to stimulate creativity are apocryphal and anecdotal. For example, Samuel Taylor Coleridge reportedly composed much of his unfinished poem *Kubla Khan* while in an opium dream. In ancient Greece, however, the

Pythian priestesses of the oracle at Delphi inhaled medicinal fumes to facilitate revelatory trances—as did the priests and peoples of most ancient societies. The institutionalized twentieth-century Native American Church continues to use the peyote of their ancestors to promote profound religious experiences.

Psychedelic drugs, such as lysergic acid diethylamide (LSD), mescaline, psilocybin, and methylene dioxyamphetamine (MDA) have been used—both legally and illicitly—to increase aesthetic appreciation, improve artistic techniques, and enhance creativity. Marijuana has been used to heighten the sense of meaning, foster creativity, and heighten perceptions (also both legally and illicitly); and alcohol has been employed by countless people worldwide to relieve inhibitions, increase spontaneity, and stimulate innovation and originality.

In the industrial West, the common belief in, and positive association between, alcohol or drug use and creativity is strengthened by the popular stereotypes of artists, writers, actors, and others in the creative and performing arts as heavy users or abusers of such substances. Despite these anecdotal claims, little scientific evidence supports the notion that alcohol and drug use actually increase creativity.

Part of the reason that creativity is attributed to drug use involves the actions of many psychoactive substances in producing altered states of consciousness. These altered states are characterized by some or all of the following features: (1) *alterations in thinking*, in which distinctions between cause and effect become blurred and in which logical incongruities may coexist; (2) *disturbances in time sense*, whereby the sense of time and chronology may become greatly altered; (3) a sense of *loss of control*, during which the person becomes less inhibited and self-possessed; (4) a *change in emotional expression*; (5) *body image change*, with a dissolution of boundaries between one's self and the world, resulting in transcendental or mystical experiences of "oneness" or "oceanic feelings"; (6) *perceptual distortions*, including illusions, pseudohallucinations, heightened acuity, and increased visual imagery; (7) *hypersuggestibility*, representing a decrease in the use of critical faculties; (8) a heightened *sense of meaning and significance*; (9) *sense of the ineffable*, in which the experience cannot be expressed in words; and (10) feelings of *rebirth and rejuvenation*. When people experience such features as these, it is understandable that they attribute creativity to certain drug experiences.

The immediate problem, however, in evaluating whether this is really so depends on the definition of creativity. At the outset, three dimensions of creativity need to be distinguished: those pertaining to the creative person, those pertaining to the creative process, and those pertaining to the creative product. If creativity pertains to an attribute of the person (e.g., original thinking), then any unusual or extraordinary experiences should qualify as "creative," even if nothing of social value emerges. If creativity pertains to a process (e.g., discovery, insight), then the testing and validation of the insights must take place as well. If creativity pertains to a product, it not only should possess some measure of social utility but should embody such qualities as novelty, surprise, uniqueness, originality, beauty, simplicity, value, and/or coherence. For both the creative process and the creative product, there is no substantive evidence to indicate that alcohol or drugs have benefit, despite the ongoing belief of many that they do. The experience of the *sense of meaning or significance* produced by drugs may have no bearing on whether that experience has *true* meaning or significance. The American philosopher and psychologist William James's claim that alcohol makes things seem more "utterly utter" is especially apt. This also happens with psychedelic drugs, which have the capacity to induce a sense of profundity and epiphany (intuitive grasp of reality), but usually without any substantive or lasting benefit or practical value.

What, then, is the actual state of knowledge about the relationship between substance use and creative achievement? What few studies exist, in fact, indicate mostly detrimental effects of drugs on creativity, especially when these substances are taken in large amounts and over an extended period of time. The results of studies on the actions of alcohol typify this. As early as 1962, for example, Nash demonstrated that small doses (about equal to two martinis) of alcohol, in normal volunteers, tended to facilitate mental associations, while large doses (about equal to four martinis) had adverse effects. With the large doses, they had more trouble in discriminating and assimilating details and performing complex tasks. In

another study, Hajcak (1976) found that male undergraduates permitted alcohol on an ad-lib basis (without limits or restraints) showed greater initial productivity than when not allowed to drink but showed decreased appropriateness and decreased creative problem solving when intoxicated.

In an anecdotal study with seventeen artists who drank, Roe (1946) found that all but one regarded the short-term effects of alcohol as deleterious to their work, but they sometimes used it to overcome various technical difficulties. The general sentiment was that alcohol provided the freedom for painting but impaired the discipline. In a more extensive study of thirty-four eminent writers, Ludwig (1990) found that more than 75 percent of artists or performers who drank heavily experienced negative effects from alcohol—either directly or indirectly, on creative activity, particularly when they did not refrain from drinking when they were working. More positive effects of alcohol were found in a small number of cases, among those who used it in moderate amounts early in their careers to remove certain roadblocks, to lessen depression or mania, or to modulate the effects of other drugs.

With many anecdotal accounts to the contrary, the weight of scientific and clinical evidence suggests that long-term alcohol and drug use exert mostly negative effects on creativity. That drugs and alcohol are used so widely within the creative arts professions seems to have less to do with creativity than with social expectations and other extraneous factors. In fact, people use pharmacological substances for many reasons other than the stimulation of their imaginations. These reasons include relaxation, the facilitation of sleep, self-medication, social rituals, pleasure, or simply habituation or addiction.

Because writers, artists, actors, or musicians may write about, portray, or act out certain aspects of their pharmacological experiences does not logically or necessarily mean that these experiences are essential for the creative process. Creative people often exploit all aspects of their experiences—whether pathological or healthy and whether drug-induced or not—in a creative way; they try to translate personal visions and insights within their own fields of expression into socially acceptable, useful, or scientifically testable truths. Without some measure of social utility, unique drug-induced experiences represent little more than idiosyncratic to quasi-psychotic productions, having value and meaning only, perhaps, to the substance user.

See also **Alcohol; Lysergic Acid Diethylamide (LSD) and Psychedelics; Marijuana (Cannabis); Mescaline; Peyote; Psilocybin.**

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CRIME AND ALCOHOL.

The relationship between alcohol consumption and involvement in crime is not a simple one. Drinking is a very common activity, and most drinking is not

followed by criminal behavior. Understanding the alcohol-crime relationship requires an identification of the drinking effects and circumstances that are related to crime. Alcohol's relationship to crime also varies by the type of crime. The major crime-type distinction is between violent personal crime (such as homicide, forcible rape, and assault) and property crime (such as burglary and larceny). In addition, driving while intoxicated is a crime, and although first offenses are usually classified as misdemeanors, repeat offenders may be charged with gross misdemeanors and felonies. Certain variables also come into play in the alcohol-crime relationship. Age and gender, for example, have a bearing on whether drinking leads to criminal behavior. Young adult males are more likely than older adult males and females of all ages to engage in alcohol-related offenses. Moreover, underage drinking is a criminal offense, as is providing alcohol to minors.

According to the available evidence, drinking is more likely to be implicated in violent crime than in property crime. Moreover, violent offenses are often thought of as "expressive" or "instrumental." Expressive violent offenses are typically those resulting from interpersonal conflict that escalates from verbal abuse to physical aggression. Such violence often involves a drinking offender or drinking by both (or multiple) parties involved. Instrumental offenses have rational goals, typified by stealing to realize the value of the stolen money or goods. Alcohol is not thought to be an important causal factor in acquisitive crimes such as theft.

Research has shown that alcohol is an important factor in the occurrence of expressive interpersonal violence, that alcohol use increases the risk of being a crime victim, that the alcohol-crime relationship is complex (involving multiple factors in addition to alcohol), and that alcohol is often blamed without justification for criminal offenses.

DRINKING AS A PRECEDENT TO CRIME

The Bureau of Justice Statistics (BJS), an agency of the U.S. Department of Justice, reviewed the role alcohol played in crime by looking at convicted offender data from 1996 (Greenfield, 1998). On an average day in 1996, an estimated 5.3 million convicted offenders were under the supervision of criminal justice authorities. Nearly 40 percent of these offenders, or about two million persons, had been using alcohol at the time of the offense for which they were convicted. Whether the offender was on probation or was incarcerated in a local jail or a state prison, all the offenders were about equally likely to have been drinking at the time of the crime. What they consumed was similar as well, with beer being the most commonly consumed alcoholic beverage—30 percent of probationers, 32 percent of jail inmates, and 23 percent of state prisoners said that they had been drinking beer either on its own or in combination with liquor prior to the commission of the current offense. Consumption of wine alone was comparatively rare among the surveyed offender populations.

Surveys of crime victims also indicate that offenders had often been drinking. The National Crime Victimization Survey (NCVS) is one of two statistical series maintained by the Department of Justice to learn about the extent to which crime is occurring. The NCVS, which gathers data on criminal victimization from a national sample of household respondents, provides annual estimates of crimes experienced by the public without regard to whether a law enforcement agency was called about the crime. Initiated in 1972, the NCVS was designed to complement what is known about crimes reported to local law enforcement agencies under the FBI's annual compilation known as the Uniform Crime Reporting (UCR) Program. Estimates from the 1998 NCVS indicate that victims of about three million violent crimes each year, or about a quarter of all violent crimes, perceived the offenders to have been drinking.

Most studies of alcohol and crime focus on offenses known to the police or on offenders serving sentences for crimes that resulted in a conviction. A notable exception is a community study done in Thunder Bay, in the province of Ontario, Canada. Pernanen (1976, 1981, 1991) collected information from a representative sample of 1,100 community residents. Among those who had been victimized, the assailant had been drinking in 51 percent of the cases in which violence occurred, and 68 percent of the time the assailant was judged to have been "drunk." Pernanen notes that the findings from the Thunder Bay study are consistent with many other North American studies using police records. Generally, half of all violent offenders have been found to have been drinking at the time of their offense.

The most common pattern found in studies of violent crimes is that 60 percent or more of the events involve drinking by the offender, by both the offender and the victim, or by the victim alone. The results of a classic 1958 study by Wolfgang indicate that the most common pattern in a survey of homicides involved the presence of alcohol for both the victim and offender.

If these findings indicated the extent to which drinking was causally implicated in violent crime, it would be remarkable. It could then be argued that alcohol accounts for a majority of violent offenses. But neither the presence of alcohol in a crime nor the intoxication of an offender is necessarily an indication that alcohol influenced the occurrence of the crime. Because drinking is such a common activity, it is likely that alcohol is sometimes simply present but not causally relevant. Drinking is also sometimes offered by offenders as an excuse for the crime, as a way of avoiding being held accountable.

ALCOHOL USE AND CRIME VICTIMIZATION

Alcohol use raises the likelihood that the drinker will be a victim of violent crime. Substantial percentages of homicide, assault, and robbery victims were drinking just before their victimization. Medical examiners have done a significant number of homicide studies by running toxicological tests of the body fluids of homicide victims. Separate reviews by Greenberg (1981) and Murdoch, Pihl, and Ross (1990) found that the percentage of homicide victims who had been drinking ranges widely, but is usually about 50 percent. Goodman et al. (1986) tested the alcohol levels of several thousand homicide victims and found that 46 percent of the victims had consumed alcohol in the period before being killed, and that three out of ten victims had alcohol levels beyond the legal intoxication level.

Roizen (1993) examined studies of alcohol use by robbery and rape victims. The percentage who had been drinking before their victimization ranged widely—from 12 to 16 percent for robbery victims and from 6 to 36 percent for rape victims. Abbey (1991) and Muehlenhard and Linton (1987) also found in their studies of date rape that both offenders and victims had commonly been drinking. Abbey suggested that drinking by either the offender or the victim contributes to rape because of the impaired communication and misperception that results from alcohol's effects on cognitive ability (among other contributing factors). Males who have been drinking, for example, may mistakenly attribute sexual intent to women whom they date.

Alcohol may increase the risk that the drinker will be a crime victim because of effects that alcohol has on judgment and demeanor. Someone who has been drinking may take risks that might not be taken when sober, such as walking in a dangerous area of a city at night. Alcohol also causes some individuals to be loud and verbally aggressive. Such a demeanor can be offensive and might sometimes precipitate physical attack.

DRINKING AND FAMILY VIOLENCE

Unfortunately, violence is common in American households, and alcohol is a contributing factor, according to research done by Kantor and Straus (1989) and Straus, Gelles, and Steinmetz (1980), among others. Hotaling and Sugarman (1986) found that alcohol appears to be most relevant to the occurrence of husband-against-wife violence. Hamilton and Collins (1981) reviewed about 25 studies that examined the role of alcohol in spouse and child abuse. They found alcohol to be most relevant to wife beating, where it was present in one-quarter to one-half of all such events. (Alcohol was present in less than one in five incidents of child abuse, however.) The most common patterns were for only the husband to be drinking or for both parties to have consumed alcohol. It was uncommon for only the wife to have been drinking. Studies also indicate that husbands or intimate partners with alcohol problems are more likely to be violent against their wives or partners.

A 1998 BJS study on the relationship between crime and alcohol found that two-thirds of victims who suffered violence by an "intimate" (a current or former spouse, boyfriend, or girlfriend) reported that alcohol had been a factor. Among spouse victims, three out of four incidents were reported to have involved an offender who had been drinking. By contrast, an estimated 31 percent of stranger victimizations where the victim could determine the absence or presence of alcohol were perceived to be alcohol-related.

Research by Jones and Schecter (1992) and Barnett and Fagan (1993) on family violence suggests that violence against women may lead to their own use of alcohol and drugs as a coping mechanism. Both drinking and drug use may be a response to the physical and emotional pain and fear that result from living in a violent relationship. Miller, Downs, and Testa (1993) found that women in alcohol-treatment programs had higher rates of father-to-daughter violence than did the women in a comparison group. These findings underline the importance of interpreting the meaning of alcohol's association with family violence (and other forms of violence) carefully. As previously noted, alcohol is often present but irrelevant to the occurrence of violence. Some recent literature on family violence indicates that alcohol use may sometimes be a response to violent victimization.

ALCOHOL AND ITS CONTRIBUTION TO CRIME

There are a number of possible explanations offered for alcohol's role in crime:

- The need for money to support drinking may cause some individuals to commit crimes to generate cash to support their habit.
- The pharmacological effects of alcohol can compromise drinkers' cognitive ability and judgment and raise the likelihood of physical aggression.
- Expectations that alcohol makes drinkers aggressive may increase the chance of violence.
- Standards of conduct and accountability for behavior may differ for sober and drunken activities, and these differences can result in an increase in the likelihood of criminal behavior after drinking.

These possible explanations are not mutually exclusive, and they all may sometimes accurately describe how drinking causes crime. Two or more of the explanations may even apply to the same incident.

Committing "income crimes," or crimes to obtain money for drinking, is not thought to be an important explanation. Although the cost of maintaining an addiction to relatively expensive drugs (e.g., heroin and cocaine) is high, the price tag for supporting heavy drinking is usually modest. In most of the United States, for example, one can support a habit of daily heavy drinking for 10 dollars a day or less. The majority of individuals could maintain such a habit without resorting to crime, although many heavy drinkers spend more than this minimal amount on alcohol. There is virtually no information in the research literature about the likelihood or frequency of involvement in income crime to support drinking, but alcohol is not thought to be a major factor in income crimes. This does not mean it never happens, however, only that it is uncommon.

If alcohol is not an important factor in the occurrence of income-generating crime, why do so many property offenders (approximately 30 percent of inmates in 1996) report they were under the influence of alcohol at the time they committed such offenses? At least two explanations are possible for the high correlation between drinking and property crime. The first suggests that the correlation is simply coincidental, not causal. A second reason (put forward by both Collins, 1988, and Cordilia, 1985) is that a property offender who has been drinking is more likely to be caught than one who is sober. This reason makes sense, based on the known impairment effects of alcohol. A drinking offender may not be as competent or careful as a sober one, so drinking offenders may be overrepresented among offenders who are caught, and thus known to criminal-justice officials.

Alcohol impairs one's cognitive abilities, including the capacity to communicate clearly and the capacity to understand the verbal and behavioral cues of others. In addition, a person whose abilities have been impaired by alcohol is less able to make decisions and carry out appropriate and effective actions. Pernanen, in his early work (1976), discussed how alcohol-impaired cognitive ability can lead to violence. When one or both parties who are interacting have been drinking, there is an increased potential for misunderstanding that can lead to conflict and that may in turn escalate to violence. One factor in such a scenario is what may be called a "reduced behavioral response repertoire." Alcohol impairs a drinker's capacity to conceive and utilize the wide range of verbal and other behavioral options that are available to sober individuals. Alcohol-induced cognitive impairment may

also diminish the drinker's capacity to foresee the negative implications of violent actions. In summary, one way that alcohol increases the likelihood of violence is through its negative effects on cognitive capacities, and these effects lead to an increased risk of violence.

It has been demonstrated in laboratory experiments that both actual alcohol use and the belief that alcohol has been consumed can raise levels of aggression. In laboratory experiments using competitive encounters between opponents in which the winner could apply an electrical shock to the loser, subjects who had been given alcohol behaved more aggressively. Evidence gathered by Bushman and Cooper (1990) and by Hull and Bond (1986) also indicates that subjects who have been told they have received alcohol, but who actually have been given a placebo, are more aggressive in their administration of electrical shocks. These findings suggest that beliefs about alcohol's behavioral effects can themselves affect behavior.

Expectations that alcohol use leads to aggressive behavior probably have sociocultural roots. Anthropologists such as Heath (1976a, 1976b) and MacAndrew and Edgerton (1969), for example, note that societies differ in the behavior that occurs after drinking. Some of these differences may be attributable to racial or ethnic differences in physiological reactions to alcohol, but it is also clear that there are normative variations in what behaviors are expected or acceptable after drinking. In fact, behavioral norms after drinking may vary within societies. MacAndrew and Edgerton note that during certain "time-out" periods, usual standards of behavior are suspended. For example, festivals or Mardi Gras celebrations are often characterized by high levels of drinking and behavior that is considered deviant or criminal during normal times.

Alcohol appears to be implicated in violence in another indirect way. Drinking is sometimes used as an excuse for crime or as a way to avoid accountability after the fact. McCaghy (1968) refers to this phenomenon as "deviance disavowal." The deviance disavowal potential of alcohol can account for a drinker's involvement in crime in two ways: Individuals may drink or say that they have been drinking as an advance excuse for their conduct, or drinking may be offered as an excuse after the fact.

CRIME AND ALCOHOL: SUMMARY

Drinking alcohol and involvement in criminal behavior frequently occur together. Some of the time alcohol has a causal role in crime, but often it is merely present. Drinking is most likely to be relevant causally to expressive interpersonal violence—including family violence. Drinking can increase the risk of being victimized as well. Drinking may also sometimes help account for the commission of crimes to obtain money to support the habit, but alcohol is not a major factor in the occurrence of income crime. Drinking leads to criminal behavior in a number of ways, including having an impact on cognition and the rules that govern behavior and accountability for behavior. The alcohol-crime relationship is complex. It is clear that drinking is rarely the only cause of criminal behavior, and that when it does contribute, it is usually only one of a number of relevant factors.

See also **Complications: Cardiovascular System (Alcohol and Cocaine); Complications: Cognition; Crime and Drugs; Driving, Alcohol, and Drugs; Driving Under the Influence (DUI); Economic Costs of Alcohol and Drug Abuse; Expectancies; Intimate Partner Violence and Alcohol/Substance Use; Social Costs of Alcohol and Drug Abuse.**

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CRIME AND DRUGS. Because of widespread public and political concern over drug-related crime, there has been an urgent need to

understand the relationship between drugs and crime. However, despite numerous studies on this topic, only since the 1980s have significant empirical advances in understanding this relationship emerged.

In a comprehensive literature review, Gandossy et al. (1980) concluded that the drugs-crime relationship was far more complex than originally believed. While acknowledging the significant contributions of previous research, the authors argued that methodological problems in the studies they reviewed had obscured an understanding of the linkage between drugs and crime. As these and other reviewers have observed, perhaps the most serious of these weaknesses was the use of official arrest records as indicators of criminal activity. Studies using confidential self-report methods in settings in which there is immunity from prosecution have consistently documented that less than 1 percent of offenses committed by drug abusers result in arrest.

Studies conducted since 1980 have relied more on such confidential self-report data, which has permitted more realistic estimates of the extent of criminality among drug abusers. In addition, victims of violent crime are now being asked whether they perceived the offender to be under the influence of drugs or alcohol. The annual Bureau of Justice Statistics (BJS) National Crime Victimization Survey asks this question of crime victims. Though a subjective inquiry, the 1998 survey revealed that 30 percent of victims could not determine whether the offender was under the influence of a substance. Of those who could make a determination, about 31 percent reported that the offender was under the influence of drugs or alcohol.

From 1987 to 2003, the National Institute of Justice (NIJ) conducted a program that obtained urine specimens from and interviewed close to half a million arrestees at 44 locations across the country. Originally called Drug Use Forecasting (DUF), in 1997 it was renamed the Arrestee Drug Abuse Monitoring (ADAM) program. The program was designed to measure drug use among arrestees by calculating the percentage of arrestees with positive urine tests for drug use. The samples were collected voluntarily and anonymously at the time of arrest in booking facilities. The ADAM program has given researchers a powerful tool for obtaining empirical evidence of patterns of drug abuse. ADAM is the only national research program studying drug use that employs both drug testing and interviews, thus giving analysts the means of assessing the validity of self-report data. Therefore, ADAM data are less susceptible to either exaggeration or denial of drug use than many other surveys. Moreover, ADAM is the only national drug research program built upon data collection at the local level. This data has revealed that there is no single national drug problem, but rather different local drug problems that vary from city to city. Unfortunately, the program ended in January 2004 due to budget problems.

THE CRIMINALITY OF DRUG ABUSERS

In examining the criminality of drug abusers, it is important to note that the onset of illicit drug use typically does not result in the onset of criminal behavior. Rather, it is the frequency, not the onset, of drug use that increases criminal activity. Furthermore, the positive relationship between drug-use frequency and crime frequency is not consistent across all types of drug use and all types of crime. Such a relationship has been observed with respect to only three types of drug abuse: heroin addiction, cocaine abuse, and multiple-drug use. In addition, such associations are more common for property crime than for violent crime.

Narcotic Drug Use. Much of the current knowledge about the relationship between drugs and crime comes from detailed self-report information on the type, extent, and severity of criminal activity of narcotic (mainly heroin) addicts. Large-scale, independently conducted studies have convincingly shown that increases in property crime and robbery, which has components of both property crime and violence, are associated with increased heroin use. Such a relationship, however, is less clear for violent crimes other than robbery.

Prevalence and Scope of Property and Violent Crime. Several key studies have revealed an exceptionally high prevalence of property crime among narcotic addicts. Anglin and Speckart (1988) found that 82 percent of a sample of 386 California male narcotic addicts reported involvement in property crime over an average five-year period of daily narcotic use. Anglin and Hser (1987) reported that 77 percent of a sample of 196 female narcotic addicts

from California admitted to involvement in property crime during an average six-year narcotic addiction period. Inciardi (1986) noted that almost all of a sample of 573 male and female narcotic abusers from Miami had reportedly engaged in theft during the year prior to interview. Inciardi also found that these individuals reported involvement in more than 77,000 property crimes (averaging 135 per subject) over a 12-month period while at large in the community. This figure included 6,669 burglaries, 841 vehicle thefts, 25,045 instances of shoplifting, and 17,240 instances of fencing stolen merchandise. While these studies varied in sampling methods and definitions of property crime (e.g., including and not including robbery), they provide evidence that a substantial majority of narcotic abusers routinely engage in property crime.

Property crime comprises a considerable portion of the crime, other than drug distribution, committed by narcotic addicts. For instance, Nurco et al. (1991a) found that of the nondistribution crimes committed by a sample of 250 male narcotic addicts during an average 7.5-year addiction period, approximately 48 percent were property crimes. Research has also consistently documented that violent crime is less prevalent and occurs with less frequency than property crime among heroin addicts. Earlier studies noted that addicts tend to prefer property crime to violent crime, and that they appear to be less violent than other offenders. While findings from later studies have continued to show that violence accounts for only a small proportion of all addict crime (approximately 1% to 3%, a rate that is much smaller than the property-crime figure), the actual number of violent crimes is still quite large because addicts commit so many crimes. For example, in Inciardi's 1986 sample of 573 Miami narcotic abusers, violent crime made up only 2.8 percent of all offenses (5% of nondistribution offenses) committed by the subjects in the year prior to interview. However, this relatively small percentage amounted to 6,000 incidents of violent crime (or 10.4 per subject, on average), since a total of 215,105 offenses were committed.

Researchers have also suggested that heavy heroin use and, more recently, heavy cocaine abuse have contributed to record numbers of homicides in large cities in the United States. The ways in which drugs can contribute to violence is the basis for a prominent theory in the drugs-crime field, discussed below.

Crime and Frequency of Heroin Use. Studies have provided consistent evidence of a direct, functional relationship between the frequency of narcotic drug use (primarily heroin) and the frequency of property crime. These investigations have employed a unique longitudinal design in which crime data are obtained for each subject over periods during which the frequency of narcotic use may vary. These studies of addiction careers reveal that property-crime rates are significantly higher during narcotic addiction periods than during periods of nonaddiction. Such a relationship tends to be linear, with the highest property-crime rates occurring during the highest levels of narcotic use (three or more times per day). In addition, although most addicts commit property crime prior to addiction, the frequency of such crime increases significantly from preaddiction to addiction, and it remains high over subsequent addiction periods and low during any intervening nonaddiction periods. While other factors also influence property-crime rates, the simplest explanation for these results is that property crime is functionally related to narcotic addiction (since addicts need cash to support their habits).

Evidence of a similar relationship between heroin use and violent crime is less conclusive. Studies have consistently shown that rates for robbery, in which there are property-crime features, are considerably higher during addiction periods than during either preaddiction or nonaddiction periods. However, when rates for composite measures of violence and rates of assault alone are examined, the relationship appears less clear.

In compiling composite measures of violence, Ball et al. (1983) found that for a sample of 243 male Baltimore addicts, the number of days on which violent crime was committed was considerably higher during the first addiction period than during the first nonaddiction period. However, in subsequent studies of 250 male addicts from Baltimore and New York City, most of whom had multiple periods of addiction, more complex relationships were observed. Over an addiction career, violent-crime rates for the total sample were significantly higher for combined addiction periods than for combined nonaddiction periods (Nurco et al., 1986; Nurco et al., 1988a). This result stemmed largely from high levels of crime

committed during the first addiction period, and violent crime actually decreased over subsequent periods of addiction, a finding that appeared to be age-related. The fact that mean rates for violence were found to be even higher for preaddiction (10 days per year) than for addiction periods (8 days per year) also reflects an inverse relationship between age and violent criminal activity.

The 1999 ADAM report on U.S. drug use of arrestees revealed that opiate use among adult arrestees was relatively low compared to the prevalence of cocaine and marijuana in the overall sample. For female arrestees, the median rate for testing positive to opiates was 8 percent in 1999, and for male arrestees it was 6 percent.

Nonnarcotic Drug Use. Investigation of the nonnarcotic drugs-crime relationship only emerged as a major research question in the 1980s. In their literature review, Gandossy and associates (1980) found that in the few studies conducted on the nonnarcotic drug-crime relationship, evidence linking the use of various nonnarcotic substances to either property crime or violent crime was weak. Another reason for the unclear relationship between nonnarcotic drug use and criminal behavior is that various narcotic and nonnarcotic drugs are often used in combination. Thus, disentangling their separate relationships to criminal activity, let alone determining cause and effect, is especially problematic. Despite these difficulties, significant advances have been made in understanding the nonnarcotic drugs-crime relationship since that time.

Cocaine. Data analyses by Johnson et al. (1991) on a nationwide probability sample of 1,725 adolescents strongly supported a cocaine-crime connection. Adolescents who reported using cocaine in the year preceding the interview (comprising only 1.3% of the sample) were responsible for a disproportionately large share of the property and violent crime committed by the sample during this period. The cocaine users accounted for 60 percent of all minor thefts, 57 percent of felony thefts, 41 percent of all robberies, and 28 percent of felony assaults committed by the entire sample.

In typological studies involving seriously delinquent youth and female crack-cocaine abusers, those subjects who reported the heaviest levels of cocaine use also engaged in substantially higher rates of property and violent crime than subjects who used crack less frequently. Among a sample of 254 youth identified by Inciardi and coworkers (1993a) as serious delinquents, the 184 crack dealers (86% of whom were daily crack users) were responsible for 45,563 property crimes (an average of 231 per user) during the year preceding the interview. In contrast, the 70 subjects who were not crack dealers and who used crack less frequently (approximately three times per week) averaged 135 property crimes per year. In addition, the heavy cocaine users averaged ten robberies per year, compared with only one per year for the remaining subjects. Similar results were reported for a sample of 197 female crack abusers (Inciardi et al., 1993b). The average adjusted annual rates for the 58 subjects classified as heavy cocaine users (8 or more doses per day) were 12 for violent crime, 14 for major property offenses, and 320 for minor property crimes. These rates were substantially higher than rates for the 90 subjects classified as "typical" users (4–7.99 doses per day). For those 49 users who took less than four doses per day, the average adjusted annual rates for violence and major property crime were less than one, and the rate for minor property offenses was 24.

Increased cocaine use among narcotic addicts has also been associated with increased property and violent-crime rates. Both Nurco et al. (1988b) and Shaffer et al. (1985) found that male narcotic addicts who had higher rates of cocaine use tended to have higher rates of property and violent crime than addicts who did not abuse cocaine.

The 1999 ADAM report found that cocaine use among adult arrestees remained high, with cocaine found in more than one-third of adult arrestees in 20 sites. There was substantial variation in the proportion of those testing positive for cocaine in the various sites, however. In three sites (Atlanta, Chicago, New York City), more than 60 percent of adult female arrestees tested positive for cocaine. In six other sites, however, cocaine use was less than 25 percent.

Other Nonnarcotic Drugs. The use of other nonnarcotic drugs appears to be unrelated to increased criminal activity. While there is considerable evidence that frequent users of multiple nonnarcotic substances,

including amphetamines, barbiturates, marijuana, and PCP, typically have high crime rates (although somewhat lower than the rates for heroin addicts), such is not the case for users of single non-narcotic drugs. Although such usage may be related to offenses such as disorderly conduct or driving while impaired, it is not generally associated with predatory crime.

Marijuana. Research on the relationship between marijuana use and crime has found that the use of marijuana is not associated with an increase in crime—with the possible exception of the sale of the drug, disorderly conduct, and driving while impaired. Some studies have reported that marijuana use may actually reduce inclinations toward violent crime.

A major problem in studying the association between marijuana use and criminal behavior is that the exclusive use of marijuana is generally short-lived. Further, like other illicit nonnarcotic substances, marijuana is often used in combination with other drugs. Under such circumstances, it is difficult to isolate the effects of heavy marijuana use from those associated with the use of various drug combinations.

The 1999 ADAM report disclosed that marijuana remained a very popular drug for adult arrestees, particularly among young males between 15 and 20 years of age. The median rate of marijuana positives for this group of arrestees in 1999 was 63 percent, compared to the overall adult male arrestee median rate of 39 percent and the overall adult female arrestee median rate of 26 percent.

Amphetamines. Literature reviews published during the late 1970s and early 1980s (e.g., Gandossy et al., 1980; Greenberg, 1976) reported that the association between amphetamine use and crime was difficult to determine because of the diversity of amphetamine users, among other factors. More recent ethnographic studies of drug abusers (e.g., Goldstein, 1986) have reported that amphetamine use is related to violent crime in some individuals. In the general population, however, the association between amphetamine use and crime is not readily apparent. Despite assertions of the media in the 1960s and 1970s, the prevalence of amphetamine-related violence among American youth is likely to be quite low.

The 1999 ADAM report indicated that methamphetamine use among ADAM arrestees was concentrated mainly in the western part of the United States. A large number of sites had virtually no presence of methamphetamine. However, prevalence rates exceeded 10 percent both for adult female arrestees in 12 sites and for adult male arrestees in 9 sites.

Psychedelic Substances. Most studies investigating the relationship between psychedelic-substance abuse and crime have involved phencyclidine (PCP). Much of this research has examined the relationship between PCP and violence. As in the coverage of many other nonnarcotic drugs, media reports, principally in the 1970s and early 1980s, have emphasized a perceived link between PCP use and violent behavior. However, the actual extent of this link has been greatly exaggerated. In his report on the subject, Kinlock (1991) noted that serious methodological problems in some studies, as well as contradictory findings in others, disallowed a conclusive answer to the question of whether PCP use increases violent crime. Nevertheless, researchers have suggested that the inconsistency of study findings may indicate that PCP use facilitates violence in a small proportion of users (see Inciardi, 1986; Kinlock, 1991). There is agreement that biological, psychological, situational, and other factors underlying seemingly drug-related aggressive behavior should be examined in future research.

THEORIES ON THE DRUGS-CRIME RELATIONSHIP

Inciardi (1986) has noted that numerous theories have been posited to explain the drugs-crime relationship. Many of these theories deal with the etiology of drug use and crime. Early etiological theories tended to be overly simplistic, focusing on what Inciardi termed the "chicken-egg" question: Which came first, drugs or crime? This question polarized the drugs-crime field for over 50 years. It typically reflected two mutually exclusive positions, with one side arguing that addicts were criminals to begin with and that addiction was simply another manifestation of a deviant lifestyle, and the other side positing that addicts were not criminals but were simply forced into committing crime to support their drug habits.

Reflecting a middle-ground position, more recent theories have argued for a diversity among narcotic addicts with regard to the predispositional characteristics and motives underlying drug-related criminal behavior. For example, based on their research with narcotic addicts, Nurco and his associates (1991b) concluded that there is considerable variation among addicts in their propensity toward criminal activity: Some addicts were heavily involved in crime prior to addiction, whereas others are extensively involved in crime only when addicted.

In the late 1970s, drugs-crime theories became increasingly complex, partly because studies tended to have fewer methodological problems that could interfere with the measurement of both drug use and crime. With improvements in techniques, researchers gradually become more aware of heterogeneity among drug abusers on many dimensions, including the type and severity of drug-use patterns and related criminal activity. In addition, more recent studies have found that drug use and crime, in most instances, do not initially have a causal relationship but are often the joint result of multiple influences. Among the many factors contributing to drug use and crime are negative family dynamics (e.g., lack of parental supervision, parental rejection, family conflict, lack of discipline, and parental deviance); association with deviant peers; school dropout, failure, and discipline problems; and early antisocial behavior. Consistent with the notion that all drug abusers are not alike, varying combinations of factors probably contribute to different patterns of deviant behavior in individuals at risk.

However, as Inciardi et al. (1993a) have noted, these theories still have some limitations. Most theories discuss drug abuse only as one of several manifestations of delinquency. Furthermore, as in earlier studies, the primary concern has been with the etiology of deviant behavior. Very little attention has been paid to explaining events that occur after the onset of drug use and criminal behavior, specifically how certain types of drug abuse increase the frequency of criminal activity. Finally, theories have typically focused on adolescence, without incorporating attributes and events that influence behavior during childhood and adulthood.

Among the most prominent theories in the drugs-crime field is that of Paul Goldstein regarding the relationship between drugs and violence. Goldstein's theory is based on his numerous ethnographic accounts of violent drug-related acts obtained from both perpetrators and victims in New York City. According to this theory, drugs and violence can be related in three separate ways: psychopharmacologically, economic-compulsively, and systemically. Within the psychopharmacological model, violent crime results from the short- or long-term effects of the ingestion of particular substances, most notably crack-cocaine and heroin. According to the economic-compulsive model, violent crime is committed as a means to obtain money to purchase drugs, primarily expensive addictive drugs such as heroin and cocaine. The systemic model posits that drug-related violence results from the traditionally aggressive patterns of interaction found at various levels within systems of illicit-drug distribution. Examples include killing or assaulting someone for failure to pay debts; for selling "bad," or adulterated, drugs; or for transgression on one's drug-dealing "turf."

Several key studies have analyzed data in the light of Goldstein's concepts. In a study of 578 homicides in Manhattan in 1981, 38 percent of male victims and 14 percent of female victims were murdered as a result of drug-related activity (Tardiff et al., 1986). The investigators contended that these percentages were higher than those previously reported in the United States. In a subsequent study by Goldstein and his coworkers (1989) involving 414 homicides in New York City that occurred over an eight-month period, 53 percent were classified by the police and researchers as being drug-related. In both studies, most of the drug-related homicides were attributed to systemic causes. Interestingly, in the former study most of the homicides involved heroin, whereas in the latter study most involved crack-cocaine.

Drug Use and High-Rate, Serious Criminality. As indicated earlier, the onset of illicit drug use does not typically result in the onset of criminal behavior. In most cases, both drug use and crime begin in the early teens. Generally, the less serious the drug or crime, the earlier the age at onset of involvement. For example, among illicit drugs, marijuana is more commonly used at a younger age than are sedatives or tranquilizers, and these drugs, in turn, are typically used at a younger age than "hard"

drugs such as heroin and cocaine. Similarly, minor forms of crime (e.g., shoplifting, vandalism) have an earlier onset than more serious types of crimes, such as assault, robbery, and drug dealing.

Most marijuana users do not become heroin addicts, and most youths who commit minor property crimes do not subsequently become involved in more serious offenses. In both instances, the salient variable appears to be age of onset: the younger the individual is when first using a "soft" drug or committing a minor crime, the more likely he or she will be to move on to more serious forms of deviance. In general, the more deviant the environment (i.e., family, peers, community), the earlier the onset of deviance.

Since 1980, independent studies have identified several core characteristics of high-rate, serious offenders. According to Chaiken and Chaiken (1990), these studies have consistently found that predatory individuals tend to commit many different types of crime, including violent crime, at high rates, and that they tend to abuse many types of drugs, including heroin and cocaine. Research findings have consistently reported that among heroin addicts, prisoners, and seriously delinquent youth, the younger a person is at onset of heroin or cocaine addiction, the more frequent, persistent, and severe that person's criminal activity tends to be. In these studies, individuals with early onsets of addiction (typically before age 16) tended to abuse several types of drugs and have disproportionately high rates of several types of crime, regardless of addiction status. Such findings have been observed in various geographic locations and are independent of ethnic group. These results are also similar for both males and females, with one notable exception: females with an early onset of addiction are more likely to commit prostitution, shoplifting, and other property crimes at high rates, whereas males with an early onset are more likely to commit violent acts.

Chaiken and Chaiken's 1982 study of over 2,000 male prisoners in three states was significant for at least two reasons. First, it challenged the long-held perception that drug abusers were less violent than other arrestees. While 65 percent of Chaiken and Chaiken's sample reported having used illicit drugs during the one- to two-year period preceding the arrest leading to the most recent incarceration, an even higher proportion (83%) of high-rate, serious offenders, who were identified as "violent predators," had used drugs during the same period. Among the offenders studied, violent predators were also most likely to have had histories of "hard" drug use (including heavy multiple-drug use and heroin addiction) and to have had an early onset of several types of drug use and criminal activity. Second, and perhaps more important, the information on an offender's drug history was more likely than official arrest records to be related to the amount and seriousness of self-reported criminal activity. As in the results of drug-crime studies discussed earlier, official arrest data were poor indicators of the type, amount, and severity of crime committed by these respondents.

These findings suggest a potential for using an individual's history of illicit drug use, including age of onset, in identifying high-rate, dangerous offenders. However, this approach has several limitations. First, a general caution is in order whenever findings based on aggregate data are applied to an individual case. Second, although self-reports of drug use and crime are generally valid when obtained from individuals who are either at large in the community, entering a drug-abuse treatment program, or already incarcerated, they tend to be less accurate for individuals being evaluated for initial disposition in the criminal-justice system. Approximately one out of every two new arrestees identified as drug users by urine testing will conceal their recent drug use, even in a voluntary, confidential interview having no bearing on their correctional status.

See also **Antisocial Personality Disorder; Arrestee Drug Abuse Monitoring (ADAM and ADAM II); Cocaine; Conduct Disorder and Drug Use; Crime and Alcohol; Criminal Justice System, Treatment in the; Families and Drug Use; Heroin; Intimate Partner Violence and Alcohol/Substance Use; Marijuana (Cannabis); Myths About Addiction and Its Treatment; Narcotic; Phencyclidine (PCP); U.S. Government Agencies: Office of National Drug Control Policy.**

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CRIMINAL JUSTICE SYSTEM, TREATMENT IN THE. In the United States, approximately 80 percent of prison and jail inmates have a history of drug or alcohol abuse and nearly one-half meet diagnostic criteria for current substance abuse or dependence. Roughly 60 percent of arrestees test positive for illicit drugs at booking. Conversely, two-thirds of clients in

residential drug abuse treatment and one-half in outpatient drug abuse treatment have some current involvement with the criminal justice system.

One-sided strategies that have emphasized either punishment or treatment for drug offenders have typically met with disappointing results. Upon release from prison, over 60 percent of drug offenders are re-arrested for a new crime, more than half are re-incarcerated, and 95 percent return to substance abuse. Moreover, simply diverting these individuals into treatment with insufficient correctional supervision has produced equally lackluster results. Nearly 70 percent drop out of treatment or attend irregularly within a few months, often well before receiving a minimally adequate dosage of treatment, and crime rates have increased in some instances.

Programs that reliably produce the most beneficial results are those that combine community-based substance abuse treatment with continuous monitoring by the criminal justice system and certain and immediate consequences for clients' failure to comply with treatment or other supervisory obligations. The basic elements of effective programs include:

- Treatment in the community. For treatment gains to generalize and be sustained, clients need opportunities to practice new skills (for example, drug-refusal strategies) in the community where those behaviors must ultimately occur.
- Opportunity to avoid a criminal record or incarceration. Treatment completion and abstinence are most attractive to clients when they are rewarded with the opportunity to avoid a serious criminal sanction and possibly the stigma of a criminal record.
- Close supervision. Programs are most effective when they can rapidly and reliably detect substance use and other infractions, when clients' progress is regularly reviewed by staff, and when team members share important information with each other, including information about treatment attendance, abstinence, and rule infractions.
- Certain and immediate consequences. The more rapidly and reliably rewards and sanctions are applied for achievements and infractions, the more effective the program.

COMMUNITY DISPOSITIONS

The unprecedented expansion of the U.S. inmate population that ensued from the War on Drugs led to spiraling correctional costs and severe prison overcrowding. This situation has left many jurisdictions with little choice but to divert large numbers of nonviolent, drug-possession offenders from incarceration to community-based correctional programs.

A relatively new but successful example of such a diversionary program is drug courts. Drug courts are special criminal court dockets that offer a judicially supervised regimen of substance abuse treatment and other needed services in lieu of criminal prosecution or incarceration. Clients in drug courts must attend frequent court hearings in which the judge reviews their progress in treatment and the results of random weekly urine drug testing and can administer punitive sanctions for infractions and rewards for accomplishments. Common examples of sanctions include verbal reprimands, writing assignments, increased drug testing, fines, community service, and brief intervals of jail detention. Common examples of rewards include praise; applause; small, token gifts; certificates of recognition; and reductions in treatment or supervisory obligations. In pre-plea or pre-adjudication drug courts, successful graduates have their charges dropped and may have the record expunged, making the arrest a legal non-event for many purposes. In post-adjudication drug courts, the conviction stands but graduates can avoid incarceration or have their probation term reduced in length or severity.

Several rigorous meta-analyses and systematic review articles have concluded that drug courts reduce substance use and crime by an average of 20 to 30 percent while participants are in the programs and reduce re-arrest rates after discharge by about 10 to 15 percent as compared to probation or adjudication as usual. The positive effects on crime have been shown in several studies to last several years after the program. Outcomes other than re-arrests (for example, substance use or employment) are difficult and costly to assess after discharge.

Other community programs have been studied less intensively than drug courts but are showing promising evidence of success. *Seamless probation* unites probation officers and clinicians as a team in the treatment and management of probationers.

The probation department might, for example, maintain office space at the treatment program and vice versa, thus reducing the likelihood of clients falling through the cracks and eluding deserved consequences, permitting a more efficient exchange of information, and allowing for co-facilitation of certain group interventions by probation officers and clinicians. Emerging evidence suggests outcomes may be substantially improved by such an arrangement; however, more research is needed to identify best practices for this approach. Some types of clients might respond well to this integrated strategy, whereas others might respond better to more traditional clinical interventions that maintain stricter confidentiality and separation of boundaries between treatment and the criminal justice system.

Coerced abstinence refers to a straightforward arrangement in which drug offenders are required to deliver randomly timed urine specimens on at least a weekly basis. They receive negative sanctions that gradually escalate in magnitude in response to successive drug-positive specimens. At higher magnitudes, the sanctions could include jail detention of up to a few days but eventually could result in a custodial sentence. Significant reductions in substance use, technical violations, and new offenses have been reported in at least two randomized experimental studies contrasting outcomes to standard probation or pre-trial supervision. More research is needed, however, to determine what types of drug offenders are aptly suited to such an arrangement. Presumably, individuals who are compulsively addicted to drugs or alcohol would have considerable difficulty stopping their usage even in response to threatened sanctions. However, individuals whose use has not yet progressed to the point of addiction and is still under voluntary control might respond sufficiently to this relatively simple and inexpensive procedure. Evidence also suggests that the use of punishment alone rarely leads to sustained improvements over the long term, and it may be as important or more important to reward offenders for engaging in productive and socially desirable behaviors in order to maintain abstinence after the coercive control of the criminal justice system has been lifted.

RE-ENTRY PROGRAMS

Less is known about successful re-entry strategies to assist inmates in returning to their communities following imprisonment. What is clear is that offering treatment behind bars without continuity of care in the community rarely elicits lasting change. The effects of in-custody treatment degrade rapidly soon after release. Importantly, however, in-custody treatment does offer important benefits. First, it is associated with fewer disciplinary infractions by inmates and greater job satisfaction by correctional officers. More importantly, it is associated with better compliance with treatment in the community following release. In-prison programming can prepare inmates to make better use of treatment services upon release, when they are at the greatest risk for relapse. In the first several months after release from prison, constraints have suddenly been lifted, the individual faces major challenges to re-engage with others, and a criminal record may pose a serious obstacle to successful re-integration (for instance, making it difficult to obtain a job or housing). Under such circumstances, a resumption of substance use or crime is often looming and a seamless transfer from in-custody to community-based treatment may be critically important to guard against impending relapse or criminal recidivism.

Unfortunately, evidence suggests the most commonly available treatments in prisons and jails are not very effective. Often going by names such as *psychoeducational groups* or *drug-focused group counseling*, the average effects of the interventions are not appreciably better than zero. Further, substantial proportions of inmates with identified substance abuse problems may receive little or no services at all. Many facilities target their scarce treatment slots to inmates who are scheduled to be released in the not-too-distant future, but who still have sufficient time left on their sentences to permit them to complete the intervention. This narrow time window, coupled with slow turnover of available slots, means that many needy individuals never gain access to the programs. In addition, it is not uncommon for some prisons to conduct "criminogenic risk assessments" of inmates and to exclude higher risk offenders (those with more serious criminal backgrounds) from participation in treatment programs. Although this may make sense from the standpoint of maintaining institutional order and control, it can also have the effect of excluding some of the most drug-addicted and impaired individuals from needed services.

The most widely studied re-entry programs are correctional *therapeutic communities* (TCs). TCs are residential programs that isolate clients from drugs and alcohol. Peers influence one another by confronting negative traits and behaviors, rewarding good performance, and offering mentorship and camaraderie. Clinical interventions commonly include process groups, milieu therapies, and community meetings, and more recently TCs have begun integrating behavioral and cognitive-behavioral components into their programs. Research reveals that in-prison TC treatment alone is insufficient to produce lasting improvements; however, offenders who begin TC treatment in prison and continue in a work-release TC program followed by outpatient aftercare have substantial reductions in crime and re-arrest rates. This step-down approach from institutional treatment to treatment in a halfway house or work-release center to outpatient treatment appears to be the most effective approach for the large proportion of inmates who may lack adequate social supports and access to sober living arrangements in the community.

MEDICATIONS

The criminal justice system has traditionally been wary about the use of anti-addiction medications. In part, this attitude may be due to ethical concerns about the coercive use of medications with prisoners and also to the fact that some anti-addiction medications, such as methadone, have psychoactive properties and are addictive themselves. However, research consistently demonstrates that maintaining addicts on appropriately prescribed medication can substantially reduce illicit drug use, crime, and HIV-risk behaviors such as needle sharing. For individuals who were prescribed medication prior to their arrest, the sudden discontinuation of treatment, substitution of a different medication, and/or lower dosage are problematic, but not uncommon, occurrences when individuals enter the criminal justice system. Moreover, for the relatively large proportion of offenders who have co-occurring psychiatric disorders, such as major depression or bipolar disorder, it may be tantamount to malpractice to discontinue prescribed psychotropic medications without a thorough psychiatric re-evaluation and medically indicated reason for doing so.

Fortunately, newer classes of medications are being developed that have less or no addictive properties and that can assist in reducing cravings or blocking the psychoactive effects of illicit drugs. Examples include naltrexone and buprenorphine, which are used to treat opioid dependence. Greater use of such medications is critically important for intervening with the large numbers of drug-addicted individuals entering and leaving U.S. jails and prisons each year.

See also **Coerced Treatment for Substance Offenders; Prisons and Jails; Prisons and Jails, Drug Treatment in.**

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CROP CONTROL POLICIES.

The crops that produce heroin, cocaine, and cannabis are respectively the opium poppy, *Papaver somniferum*; the coca bush, *Erythroxylum coca*; and the three cannabis plants—*Cannabis sativa, Cannabis indica,*

and *Cannabis ruderalis,* the most widely grown of which is *Cannabis sativa*. Crop control policies have included a wide range of strategies, from diplomatic pressure to enforced eradication.

The most difficult crop to control is cannabis because it can grow almost anywhere in the world, even in altitudes of up to 8,000 feet. Its life cycle is only three to five months, so it is quick to grow and easy to harvest. Modern techniques mean that it can be grown indoors hydroponically, as well as outdoors, but for increased potency, it needs full sun and warmth. There has recently been a dramatic change in the illicit cannabis market as the drug is increasingly produced locally rather than trafficked from one country to another. Vietnamese gangs have been found in the United States, Canada, and the United Kingdom running massive indoor cannabis farms with as many as 17,000 plants. Eradication of cannabis is therefore more of a domestic or national problem.

The opium poppy is similarly ubiquitous, although yield varies with weather and conditions, and it needs enough sun and water for maximum yield. Turkey was the traditional supplier for Europe and the North American eastern seaboard via the infamous French Connection, where Turkish opium was processed by French criminals based in Marseilles. When Presidents Nixon and Pompidou acted in concert to close down the trafficking route, production increased elsewhere, particularly in Mexico and in the *golden triangle* of Laos, Thailand, Myanmar (Burma), and part of the bordering Yunnan province of China. Other contributors were the *golden crescent* countries of Iran, Pakistan, and Afghanistan, although Iranian production all but ceased after the United States and Britain made this a condition of restoring the Shah of Iran to the Peacock Throne. Political pressure on Thailand produced the same result. This left Afghanistan and Pakistan the major producers at that time.

By contrast, the coca bush—a perennial with a life span of up to forty years and up to six harvests a year of its leaves—is geographically specific, with the warm, humid eastern slopes of the Andes at between 4,500 and 6,000 feet ideal for growing, either in open spaces or as understory in the forest. Peru and Bolivia were the major producers with a small amount grown in Ecuador until Colombian cocaine drug trafficking cartels in Medellin and Cali started taking control of distribution and then began growing it themselves. They later diversified into opium poppies and heroin.

Two other plants are less widely used as mild stimulants, namely khat (sometimes spelled qat), *Catha edulis*, and ephedra, *Ephhedra equisetina*. Khat contains the alkaloid cathinone, which itself is under international control, but in many countries the khat tree and its leaves are not. It is grown in Yemen and Somalia and, because it has become more profitable than coffee, Kenya. Its use is mainly limited to the Yemeni and Somali communities, and little if any effort is made to control its growth since the active ingredients disappear little more than a day after picking: Customs officers can merely delay shipments for a week before releasing them. There is also relatively little concern about the ephedra plant, a source of ephedrine, because ephedrine and amphetamine are made predominantly in laboratories.

Although there are also thousands of plants, roots, leaves, flowers, nuts, and mushrooms with psychoactive and hallucinogenic properties, most often they are gathered rather than farmed. Only the poppy, coca bush, and cannabis plant are illegal in volume production. As of the early twenty-first century, the main world producers of heroin and cocaine were Afghanistan and Colombia respectively.

EARLY EFFORTS TO STOP OPIUM PRODUCTION

There are two direct examples of opium poppy eradication as a result of political pressure, namely in Turkey and Iran, but in neither case was the eradication sustained.

Turkey's Exit from Opium Production. In 1969 two new presidents took office, Richard Nixon in the United States and Georges Pompidou in France. Pompidou wanted to repair relations with the United States and at the same time clean up the Service de Documentation Extérieure et de Contre-Espionnage (SDECE), the French intelligence service, and the Service d'Action Civique (SAC), a force originally set up to protect President Charles de Gaulle. The latter employed men involved in the heroin trade for dirty work. After a slow start, arrests accelerated after a man who had worked for SDECE was found with 45 kilos of heroin in his campervan in New Jersey.

Meanwhile, the United States had launched Operation Intercept in September 1969 to stop cannabis and heroin from coming into the country through Mexico. At the time, the Mexican ruling elite were tied to the French heroin business. However, almost no drugs were seized, and the operation proved a diplomatic disaster with Latin America as a whole, so the operation was quietly dropped (Musto & Korsmeyer, 2002).

Eager to make a political impact on illicit drugs, Nixon turned his attention to Turkey, a NATO ally that grew no more than eight percent of the world's total opium, but was diplomatically, politically, and physically accessible in a way that opium producers such as Afghanistan, Burma (Myanmar), India, Pakistan, and Thailand were not. Following a military coup in 1971, the new regime, headed by Nihat Erim, traded arms and American aid in exchange for suppressing poppy growing. The package included $35 million in compensation to farmers. The policy worked through a combination of military control and easily accessible growing areas. There was little global effect, however: Production increased in Mexico and the Far East to fill the gap in the market. Nor was Turkey's expertise lost. In July 1974 it resumed production under government control because of a world shortage of codeine. Controllability was the key here. Australia also helped fill the medical gap by offering Tasmania as a safe and secure place to grow legal opium.

Iran, the Shah, and Oil. In 1953 Mohammad Mosaddeq, the prime minister of Iran, was ousted in a western-backed coup, and Shah Mohammad Reza Pahlavi was restored to the ancient Peacock Throne that he had occupied since 1941, thus safeguarding Western interests in the country. Abolition of opium poppy cultivation was a condition of his restoration, and this was achieved in 1955 using military force. The Shah, however, decided in 1969 to replant 20,000 hectares with opium poppies for sale to registered addicts to control a developing problem. Opium had been coming into the country from other producers and turned into heroin, thus creating heroin addicts instead of opium smokers and opium addicts. The fall of the Shah in 1979 and the takeover by religious leaders meant that, once again, opium production was eradicated and therefore no estimates exist of any illegal opium growing. Anecdotal evidence suggests a small but increasing amount might be grown, but Iran's contiguous borders with Afghanistan and Pakistan means there is no difficulty in getting supplies of illicit opiates into the country.

THAILAND AND PAKISTAN

Political pressure was also exerted on Thailand and Pakistan to reduce illicit opium production. In Thailand peasants grew opium in the highlands, but the Nationalist Chinese Army, the Kuomintang (KMT), the remnants of Chiang Kai-shek's army defeated by Mao Tse-tung in 1948, controlled the trade. Heavily involved in the opium trade in China, they trafficked opium from Burma until 1961, when they were forced out and moved to Thailand. Mule caravans moved the opium grown in northern Thailand to Bangkok, where it was processed into heroin. Thailand announced an anti-opium program in 1969 but, due to the communist insurgency and widespread corruption throughout the government, it took 30 years to get production down to nine metric tons in 2001, the last year for which figures are available (World Drug Report, 2008). Only after the insurgents were defeated and widespread alternative livelihoods programs put in place was eradication of the opium poppy possible.

In Pakistan numerous alternative development programs were tried, particularly in the Dir valley, but the net result was that the valley became depopulated. In 1990 it produced 7,488 metric tons. This fell to 260 metric tons by 2000, but production began rising again and reached 1,701 metric tons in 2007, mainly in tribal areas near the Afghan border.

AFGHANISTANI RISE IN OPIUM PRODUCTION

Afghanistan produced 8,200 metric tons of opium in 2007, compared with 460 from Myanmar, 9.2 from Laos, and only 3.2 from Thailand. Afghanistan topping the opium production table is largely an unintended consequence of U.S. foreign policy. The United States backed Mujahideen resistance to the Soviet Union invasion of Afghanistan in 1979 by using drugs, which had undermined U.S. forces in Vietnam, as a weapon. With Saudi Arabian financial backing and logistical support from a strongly Islamist Pakistan, production of opium and cannabis was encouraged at the expense of traditional crops such as wheat and apricots; the Afghans even halted fighting invaders to

harvest the crop (Cooley, 1999). When the Soviet Union withdrew in 1989, civil war broke out between Afghan warlords, and in 1994 the Taliban moved in with the connivance of the Pakistan intelligence service, the Directorate for Inter-Services Intelligence (ISI), and Saudi financial support. In the hope of gaining international recognition for their regime, Taliban leaders stopped all opium growing in 2001, on pain of death, so farmers starved and/or went into serious debt. But when international recognition did not come, the Taliban let production resume.

The net result is that Afghanistan has become a narco-state, with an estimated 60 percent of gross domestic product (GDP) generated by drugs. Partly because of history, trying to eradicate opium production posed major problems that were compounded by the complex nature of the country. There is no one common language, although Pushtu, Dari, and Urdu are most common, and the country has nine different ethnic groups or tribes—Uzbegs, Hazaras, Turkmen, Tajiks, Aimaq, Kirgiz, Nuristani and Pashtoons (or Pathans), five of which straddle the borders. There are also nomadic groups such as the Ghilzai. The border with Pakistan is a particular problem: Drawn by the British in 1893, it placed all defensible foothills in what is now Pakistan. This cut the Pashtoon (Pathan) nation in two, so the border is not recognized by the Pashtoon, and its mountain ranges are completely porous and unpoliceable. In addition, in some tribal areas in Pakistan along the Afghan border, local leaders rule themselves.

With widespread poverty and many farmers dependent on the opium poppy, the effects of eradication would be devastating. Therefore the issues surrounding the eradication (physical destruction of the standing crop) or elimination (no longer grow the crop) are intimately tied to the role of opium in the economy.

ERADICATION, CROP SUBSTITUTION, AND ALTERNATIVE DEVELOPMENT

The United Nations Fund for Drug Abuse Control (UNFDAC), one of the predecessor bodies of what is now the United Nations Office on Drugs and Crime (UNODC), was set up in 1971 to control the supply of drugs and establish crop substitution programs in Pakistan and Latin America. For many reasons these programs were a complete failure, with farmers either taking the money for not growing the crop, then growing the illicit crop in different areas, or finding the alternative crop impossible to market. Examples include truckloads of tomatoes rotting because a landslide prevented the trucks from reaching the market, or fruit ripening during a glut in the market, or a cheese factory being set up where people do not eat cheese or keep goats or cows.

The concept changed to *alternative development* (AD) which "sought to create an economic and social environment in which households can attain an acceptable standard of living without the need for drug crop cultivation" (Mansfield & Sage, 1997, p. 166). However, implementation suffered from a too uniform approach that failed to take into account the diversity of the population such as land ownership, or lack of it, the mobility of some workers, and the role of opium in households. In addition, the idea had been based on the simplistic assumption that behavior is driven only by economic rationality, with other factors playing no part (Mansfield, 2007).

Conditional on giving aid for alternative development, the United States has often argued for a parallel program of poppy eradication by spraying with glycosaphate, or Round Up, as is done in Colombia. However, there is little evidence that eradication reduces cultivation in the long term—drug crops move, production technologies evolve, and total production decreases very slowly if at all. It damages communities without undermining the reasons why people choose to grow drugs, and "there is no evidence... that it is possible to rebuild economies quickly" (UNODC, 2005, p. 23). In other words, this *conditional development* has failed.

The UNODC (2005), therefore, says alternative development should be used in four different ways, namely as a "multifaceted holistic, systemic, strategic approach to a complex problem... (as) the leg of a stool with interdiction, policing, eradication and education as the other legs... (as) a series of discrete development projects or pilot projects... (and) no more than a new name for crop substitution" (UNODC, 2005, p. 18). It notes that in Lao People's Democratic Republic, Pakistan, Vietnam, and Latin America poorly designed alternative development projects led to an increase in cultivation so that the

farmers could earn enough to participate in projects to reduce the drug crop. Similar faults were evident from the 1970s UNFDAC projects in Pakistan and the Hindu Kush.

SUSTAINABLE LIVELIHOODS

The concept of sustainable livelihoods dates from 1987 and was developed by Chambers and Conway in 1991 and then taken up by the U.K. Department for International Development (DFID) and later by the U.S. International Narcotics and Law Enforcement Bureau (INL). The DFID definition (1999–2001) is that "a livelihood comprises the capabilities, assets, and activities required for a means of living. A livelihood is sustainable when it can cope with and recover from stresses and shocks and maintain or enhance its capabilities and assets both now and in the future, while not undermining the natural resource base" (DFID, 1999–2001). As a concept it has been endorsed by the World Bank with the proviso that it is mainstreamed into rural development programs (Ward & Byrd, 2004).

AFGHANISTAN NATIONAL DEVELOPMENT STRATEGY

The Afghan government has proposed the systematic integration of the counter-narcotics dimension into all policies, strategies, programs, projects, studies, and technical assistance. They argue that alternative livelihoods and law enforcement against traffickers and processors must go together but that eradication should only come in once these have been established (Afghanistan National Development Strategy, 2006). How realistic this is when set against a likely unachievable goal of a 70 percent reduction in production by 2008 and elimination by 2013 remains to be seen as pressure to eradicate runs ahead of establishing alternative livelihoods. However, it is clear that this strategy will take many years to implement, but it seems to be the only viable one. There is also the problem of how to deal with powerful local warlords or clan chiefs, who might wish to undermine all the central government's initiatives. One way might be to incorporate them into the antidrug effort through economic support, in return for aid in implementing the strategy.

AID DIFFICULTIES IN AFGHANISTAN

With international aid accounting for 90 percent of all public expenditure funding in the early 2000s, the Afghan government does not know how some $5 billion has been spent, owing to a lack of communication and coordination. More than two-thirds of all aid bypasses the Afghan government. In addition, many countries pledged funding for projects but have not honored their commitments, causing a $10 billion shortfall on promised aid. Additionally, over half the aid is tied, requiring the procurement of donor-country goods and services. Thus, 45 percent of tied aid goes back to donor countries in corporate revenues and consultant salaries, where the profit margins range from 20 percent to 50 percent (Waldman, 2008). There are substantial "aid gaps," and many donors are suspicious of giving aid because of corruption within the government and among the governors in the country.

A further complication is the lack of a legitimate banking system, which makes aid difficult to distribute and the proceeds of drug trafficking impossible to trace. There is monetary exchange, but via the Hawala system, an informal network of trusted individuals who guarantee receipts and payments among themselves. This system operates also in Pakistan, Bangladesh, China, and Saudi Arabia (Maimbo, 2003, Thompson 2007). A government controlled banking system that works and that users trust is needed, possibly combining the advantages of the familiar Hawala system, but providing transparency for the transfer of funds.

ALTERNATE SOLUTIONS TO OPIUM PROBLEMS

A number of methods have been proposed to curb the production of illegal opium crops, but none of these approaches has met with long-term success.

Specially Bred Weevils. Numerous diseases (mildew, blight) and insects (aphids, thrips, and cutworms) attack the opium poppy (Kapoor, 1995), but the strangest story associated with opium parasites is that of the screwworm. In 1971 President Nixon appointed Jerome Jaffe, a noted treatment specialist and pharmacologist, as the first national Drug Czar to head the Special Action Office on Drug Abuse Prevention (SAODAP). The president suggested that they find an insect that could consume poppy crops. To limit proliferation, it would have to die after intercourse, so it was dubbed the screwworm. The job was given to the Department of

Agriculture Stoneville (Mississippi) laboratories, where scientists experimented with various weevil life cycles. Two problems occurred: First, no one could guarantee that the weevil would be specific to opium poppies and would not eradicate wheat or rice crops as well; second, it could not be confined to illegal crops, but could spread to legal opium crops, the source of morphine, thebaine, and codeine. This could cause a worldwide health crisis in pain control, with international repercussions. "The screwworm was relegated to a long-term experimental program which would be made operational only if it produced a categorically host-specific weevil that would also stop at international borders" (Epstein, 1977, p. 151).

Pay Farmers Not to Grow. In 2002 the United Kingdom offered Afghan farmers $1,235 per hectare not to grow opium poppies. If they had grown wheat instead, they would have added an income of $390 per hectare. Even in a bad year—2004, for example—gross income per hectare from opium was still $4,600. In 2003, a good year, the yield was $12,700. Also, many farmers never received the promised money for not growing opium, resulting in a legacy of a long-term lack of trust.

Buy the Opium Crop. The recent suggestion of the Senlis Group (2005), which licenses exports of opium for pain relief in Africa, would offer a short-term solution, but is based on a false assumption that there is a world shortage of such opiate-based analgesic medicines. According to the International Narcotics Control Board (INCB), which licenses controlled opium production for medical purposes, this is no longer true, although it might have been in 1989, when a joint WHO-INCB report looked at the problem. But by 2007 the same organizations concluded that the current supply of legal opium was adequate to meet world demand. Although more painkilling drugs might be needed in Africa, they are not being used or prescribed for various other reasons. To change this culture would take years, and the lack of a regulatory framework or a secure distribution network in many less-developed countries could lead to drug diversion into illicit markets.

Moreover, if Afghanistan were to overprovide for the opiate needs of the world, what would happen to the Tasmanian, Turkish and Indian farmers who have licences to supply medical markets already? Would their livelihoods be taken away?

Seed with Low-Morphine Poppies. Another suggestion involved sowing poppies with lower morphine yields, such as *Papaver bracteatum* (now called *orientale*), which has a high yield of thebaine and low morphine content. Also it does not fall under the control of the 1961 Single Narcotic Convention or its amended 1972 list. However, thebaine is source of the so-called Bentley compounds, discovered in 1963 by the pharmacist K. W. Bentley. One of these, etorphine, is 1,000 times more powerful than morphine. This plan was not pursued.

Close Down Laboratories. One idea favored by the United Kingdom is to use Special Forces to target the laboratories where opium is converted into heroin. However, a laboratory can be a room in a house, a courtyard, or a cave. All producers need are filtering cloths, two barrels, and various easy-to-obtain chemicals (Zerrell et al., 2005). The only one that may be difficult to obtain is acetic anhydride, but drug refiners appear to have no problem procuring this. Heroin can be processed easily in small batches using hundreds of makeshift, temporary laboratories, each operating for a few days at a time. With risks spread in this way, closure of a few small units, when found, would have little impact on total production.

Spray the Poppy Fields. The fungus that attacks poppies, *Pleosporum papaveracea*, has been well researched, but there is a fear that it may well damage other crops. *Denryphion penicillatum* is also a pathogen for poppies. But the fungi that attack poppies, coca, and cannabis have been genetically modified, so these agents might also attack other vegetation and possibly damage human and animal life, leading to a consequent reluctance to use them.

COLOMBIA, COCA, AND HEROIN

Similar arguments to those in Afghanistan apply to Latin America, where, in 2007, Colombia had 99,000 hectares under coca cultivation; Peru, 53,700; and Bolivia, 28,900; producing 600 metric tons, 290 metric tons, and 104 metric tons, respectively to produce a grand total of 994 metric tons (UNODC, 2008). Colombia also produced 14

metric tons of opium. Claims of reduced cocaine production though eradication are difficult to prove. With no obvious shortage of cocaine on the world markets, many commentators suggest that the coca bush is simply being planted in new areas (National Drug Intelligence Center, 2007).

Alternative development. Alternative development has been tried in Colombia, particularly in the Chapare region and Upper Huallaga Valley. However, projects were individual rather than systematic and rounded packages of aid and were not linked with long-term development plans. The result in some places has been a disproportionately negative impact on the poor, forcing many people from their farms and villages into the favelas of the towns.

Spray with Herbicide or Fungus. As part of Plan Colombia, funded by the U.S. government in 2000, the herbicide *glyphosate*, or Round Up, was used to kill the coca bush. The U.S. government also had an agreement with the government of Peru to test tebuthiuron—Spike or Graslon—but concern about its wider impact has inhibited its use.

Environmentalists argue that Spike is a particular risk to the ecosystem (Solomon et al., 2005). Moreover, eradication usually leads to more forest clearing and burning, as well as the displacement of farmers, to enable illegal coca bush cultivation elsewhere (AIDA, 2005; Transnational Institute [TNI], 2005). Meanwhile, the U.S. government is growing coca bushes to test means of eradication.

The fungus *Fusarum oxysporum*, which has also been genetically modified for greater impact, is fatal to both coca bushes and cannabis plants. It has been used to spray coca bushes, but the practice was banned by Latin American countries and was stopped by President Clinton. However, the United States is talking about using it again.

UNITED STATES INFLUENCE

The United States has always had more important international goals—such as the suppression of communism or the fight against terrorism—than trying to control the international drug trade. Paradoxically then, the United States has sometimes been more instrumental in the growth of drug production and drug trade than in its suppression. The United States has long supported people and states involved in illegal drugs when this has been politically expedient, going back to the invasion of Sicily in World War II, when Lucky Luciano negotiated with the Mafia for Patton's troops to pass through the island unhindered, with his eventual reward being deportation to Italy. The Mafia, who had been purged by Mussolini, was able to regain its grip and establish a postwar heroin empire (McCoy, 2003). Three other major interventions that resulted in increased opium production were in Laos in the 1960s, Vietnam in the 1970s, and Afghanistan in the 1980s. In Laos and Vietnam, the CIA were directly involved in the heroin trade, and when the agency withdrew in 1971–1972, the trade expanded to fill the Turkish gap. In Afghanistan, after the Russian invasion of 1979, the trainers of the Mujahideen (mainly the Pakistan intelligence service, the ISI, with U.S. backing) encouraged the expansion of opium and cannabis cultivation to undermine the Russian troops as the Americans had been undermined in Vietnam (Cooley, 1999). The active role of the CIA between 1981 and 1986, when cocaine trafficking helped finance the Contras in fighting the left-wing government of Nicaragua, is well laid out in the Kerry Report (1989), ranging from protecting informants, even if they were serious drug traffickers, to actively helping their activities (McCoy, 2003).

CONCLUSIONS

The provision of alternative livelihoods seems the only, but very long-term, solution to stopping cultivation of illicit drug-producing crops. If farmers' incomes increase through other means, there would be a disincentive to grow illicit crops. Simple eradication by hand or by using fungi or herbicides has not worked in the past, though there remains strong support for such policies in the United States. Experience also shows that insurgencies must be overcome before alternative development can take place, which has clear lessons for Afghanistan and Colombia in the early 2000s. One risk is that a long-term strategy based on alternative livelihoods may not survive if eradication is not carefully controlled, particularly if spraying is used. Aerial spraying of crops in Afghanistan, for example, might result in both mass starvation and an uprising. Meanwhile, simple crop substitution has proved uneconomic for farmers. Other indirect

means to reduce the drug supply are to control the precursor chemicals used in the processing of the crop and to close down processing laboratories. In Afghanistan, the lack of a formal banking system adds to the problems. In other countries the Hawala banking system or the Black Peso (its Latin American equivalent) frustrate attempts to damage drug profits through control of money laundering. Economists talk of a 10- to 20-year time frame to get rid of illicit crops, but this will require a commitment from donor countries, one that many do not think can be sustained.

See also **Afghanistan; Amphetamine; Bolivia; Cannabis, International Overview; Cannabis Sativa; Coca Plant; Coca/Cocaine, International; Cocaine; Codeine; Colombia; Foreign Policy and Drugs, United States; France; Golden Triangle as Drug Source; Hallucinogenic Plants; Heroin; India and Pakistan; International Control Policies; International Drug Supply Systems; Kenya; Khat; Mexico; Morphine; Operation Intercept; Opiates/Opioids; Opium: International Overview; Peru; Plants, Drugs From; Psychoactive; Vietnam War: Drug Use in U.S. Military; World Health Organization Expert Committee on Drug Dependence.**

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CINDY FAZEY

CULTS AND DRUG USE. *Cult* most commonly denotes a small, extremist offshoot from an established religion or other ideology. The term has pejorative connotations. Groups that are termed cults usually have a dogmatic ideology, are isolated from the outside world, have charismatic (and sometimes messianic and grandiose) leadership, and induce altered states of consciousness via exhaustion and other privation. Member identity is greatly transformed, often through a religious conversion experience, and it is expected that members will make a significant commitment. Cult is also used alternatively with the term *sect*. In recent decades the concept of sects and cults has been expanded to include nonreligious groups such as political cults (for example, the Symbionese Liberation Army) or psychotherapy cults. It is difficult at times to recognize a cult in the early activities of what will later become an established religion, and to distinguish full-fledged cults from organizations and movements that have some cultlike features.

HISTORICAL BACKGROUND

In Islam, alcohol is forbidden, but medieval Islamic sects were formed that used hashish (a form of Cannabis sativa or marijuana). The drug came into use in the Islamic Middle East only centuries after the Prophet Muhammad (who lived from approximately 570 CE to 632 CE) and his followers founded the Muslim faith. Hashish was allegedly used to offer a taste of the paradise to come.

In pre-Columbian America, drugs of a wide variety were utilized in religious rituals. The Native American Church continues to use the hallucinogens peyote and mescaline (both derived from the small cactus Lophophora williamsii). Recent court decisions have protected and reaffirmed the right of this church to use these drugs in religious ceremonies. As Preston and Hammerschlag (1983) have noted, this use of hallucinogens is rigidly controlled—part of a transcendent experience, accompanied by rituals of purification, and not lending itself to use on a promiscuous basis. Some Native American drug counselors have been members of the Native American Church, and peyotism has been a pathway from alcoholism within several tribal cultures.

Recovery from alcoholism occurred in *revitalization* movements or cults such as that founded by Seneca prophet Handsome Lake in upper New York State in 1799. Among such tribes depression and excessive drinking were endemic as they faced the humiliation and stress of deculturation under European rule.

Bohemian and countercultural subcultures have favored using psychoactive substances to alter consciousness. These groups ranged from the Parisian bohemians of the mid-nineteenth century, through the Greenwich Village bohemias at the turn of the twentieth century, the Beats of the 1950s, and, most famously, to the hippie counterculture of the 1960s and early 1970s, which overlapped with various guru-led Hindu and Buddhist philosophies.

The 1960s and 1970s were characterized by a youth movement (the baby boomer generation of the early twenty-first century) that developed an intense interest in the cultic and the occult—and by a popularization of drug use within mainstream American society. Some of this interest was fueled by the philosophies and practices of Asia, especially Southeast Asia, where the Vietnam War raged; some of it was inspired by the Shangri-La nature of the lands of the Himalayas, where Buddhism was practiced in secluded monasteries and nirvana was sought. As the greening of America proceeded throughout these two decades, mind-altering substances joined alcohol and nicotine as drugs of choice, at once available on the street and no longer confined to the disenfranchised or marginal.

More than 900 members of the People's Temple died by mass suicide/murder on November 18, 1979, in Jonestown, Guyana. The leader, Jim Jones, had lured many people into the cult by claiming he would cure their drug abuse problems. © BETTMANN/CORBIS

Increasingly, the so-called transcendent or mind-expanding religious experience was juxtaposed with drug use that often evolved into drug abuse. There was a paradoxical, parallel development of inner exploration and discovery in the then popular encounter group culture, and in the mind-altering, sleep-deprived marathon group therapy sessions that flourished in both the encounter culture and the therapeutic community's drug rehabilitation settings, which sometimes in their emotional extremism served to isolate members in a subcultural, cultish cocoon.

By combining aspects of their own experimentation with hallucinogenic drugs with elements of transcendental meditation in their 1967 song "Lucy in the Sky with Diamonds," the much beloved Beatles (who performed as a group from 1960 to 1969) both mirrored and promoted the use of hallucinogens as providing a readily accessible transcendental experience—although in Buddhism the goal of all existence is a state of complete redemption (and nirvana is a state achieved by righteous living not drugs). Unlike Aldous Huxley (1894–1963), who combined his interest in Vedanta (an orthodox system of Hindu philosophy) with the use of mescaline, the Beatles and their spiritual mentor, the Maharishi Mahesh Yogi, proclaimed the desirability of enlightening the masses rather than restricting enlightenment to a righteous educated elite.

The relationship of such cults to drug use is paradoxical. Deutsch (1983) has noted that prolonged drug use may encourage this type of cult affiliation, and many cult groups offer themselves to the public and to those most vulnerable as quasi-therapeutic environments where individuals will be able to transcend the need for drugs. A variety of cult and cultlike pathways out of substance abuse exist. In the 1960s many drug abusers overcame their addiction after joining the Hare Krishna cult, and in the 1970s many others quit by responding

to the evangelical appeals of the ultra-Orthodox Lubavitcher branch of Judaism. The Hare Krishna experience was a cult alternative to drugs that incorporated certain aspects of the counterculture valued by youth. Other movements that prospered in recruiting confused and burned-out drug users were fundamentalist Protestant groups (so-called Jesus freaks), the crypto-Protestant Children of God, and the Reverend Sun Myung Moon's Unification Church. For adolescents in the mid- to late twentieth century cult affiliation often offered a resolution of ambiguity, ambivalence, and dissonance; a small and manageable, nurturing social universe; the structured regulation of impulsivity; and a higher purpose, meaning, and identity as opposed to malaise and drift.

One charismatic cult leader was the Reverend Jim Jones, leader of the People's Temple. His claim of curing drug abuse was only one of the cult's lures. After moving around in the United States, he brought his followers to Guyana, South America. There, in a remote location, one of Jones's former substance abusers mixed a massive batch of poisoned Kool-Aid for the cult's final event—a mass suicide.

Scientology has its own chain of drug treatment programs, Narcanon, that is easy to confuse with Nar-Anon (a fellowship of relatives and significant others of addicts) or mistake as an abbreviation for Narcotics Anonymous. Its treatment of substance abusers reflects the Dianetics-based teachings of L. Ron Hubbard (born Lafayette Ronald Hubbard, 1911–1986), an American science fiction writer, whose Scientology movement expanded in the 1950s when he moved to England (he was subsequently banned from reentering England in 1968). Scientology is a quasi-philosophical system that claims to improve its followers' mental and physical well-being as they advance within the cult after completing (and paying handsomely for) a series of courses.

TWELVE-STEP PROGRAMS

Intense religious commitment is a significant aspect of much of the twelve-step recovery movement. As a result, some observers have expressed concern that this level of commitment to a program can lead to a kind of cult affiliation. Alcoholics Anonymous (AA), the oldest, most constructive, and most respected of the twelve-step programs, is not considered a cult by most, although there are several critics who so define it (Bufe, 1998). Another, more nuanced view is that for some individuals only, AA (or its sister organization Narcotics Anonymous, NA) becomes the functional equivalent of a cult affiliation, where any and all competing philosophies are defined as heretical, and all behavior is interpreted through a dogmatic lens.

THERAPEUTIC COMMUNITIES

Rebhun (1983) and many others have noted the danger that drug treatment programs can turn into cults. One such example is Synanon. Founded in 1958 by Charles A. Dederich, Synanon involved an insular, dogmatic, and rigid subculture, one ruled by an absolutist leader. Dissent was not tolerated, and violence against critics eventually resulted in the downfall of the organization. Synanon was not unique; the history of residential drug treatment centers includes a number of insular, authoritarian and hierarchical organizations. Recovering substance abusers often found it very difficult to leave the protection of a therapeutic community to become independent members of mainstream society. The therapeutic communities of the early twenty-first century have greatly modified the harsh practices of decades ago—they embrace professionalism and evidence-based practices, and encourage reentry into society via vocational and educational training. Psychotherapeutic programs through which persons have ended substance use but which former members allege to be cults or cultlike include the Upper West Side Sullivanians, Erhard Skills Training (EST), Landmark, Harvey Jackin's Re-evaluation Counseling, and Fred Newman's Social Therapy.

ASSESSMENT

Drugs and other mind-altering substances have formed an integral part of some cultic or religious rituals from very ancient times. In the mid- to late twentieth century the structure provided by groups that mobilize intense religious or quasi-religious feelings has sometimes enabled vulnerable individuals to transcend their personal difficulties such as drug and alcohol use. However, this may come at the cost of losing personal identity, fusion with an

authoritarian and charismatic leader, and loss of contact with mainstream society, family, and peers.

See also **Religion and Drug Use.**

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Encyclopedia of Drugs, Alcohol & Addictive Behavior

Third Edition

HENRY R. KRANZLER & PAMELA KORSMEYER

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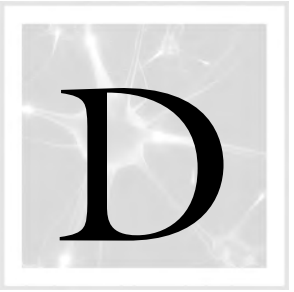

DAST. *See* **Drug Abuse Screening Test (DAST).**

DELIRIUM. The primary clinical feature of delirium is the disturbance of consciousness and/or attention. Associated symptoms are disorientation, memory deficits, and language or perceptual disturbances. Any cognitive function may be affected. Fleeting false beliefs, including paranoid ideas, are common but usually short-lived. Additional clinical symptoms include sleep/wake cycle disturbances (insomnia, daytime drowsiness, sleep/wake cycle reversal, nocturnal worsening of symptoms), increased or decreased psychomotor activity, increased or decreased flow of speech, increased startle reaction, and emotional disturbances (irritability, depression, euphoria, anxiety, apathy). Delirium develops within hours to days, and its symptoms fluctuate over time. Although many cases of delirium resolve promptly with the treatment of the underlying cause, symptoms may persist for months after treatment, especially in the elderly. Sometimes an episode of delirium establishes a new, lower cognitive baseline.

Regarding epidemiology, the community prevalence of delirium is age-dependent: 0.4 percent in those over 18, 1.1 percent in those over 55 and 13.6 percent in those over 85 (Folstein, Bassett, Romanowsk, et al., 1993). Delirium is common in the hospital setting: 11 to 42 percent. Among the elderly presenting for hospital admission, 24 percent of community dwelling and 64 percent of nursing home residents are delirious. Delirium is associated with increased morbidity and mortality. For example, 25 percent of elderly patients with delirium during hospitalization die within six months after discharge (American Psychiatric Association, 2000).

Risk factors associated with delirium are as follows: age over sixty-five, physical frailty, severe illness, multiple diseases, dementia, visual or hearing impairment, polypharmacy, sustained heavy drinking, renal impairment, and malnutrition. Precipitants are acute infections, electrolyte disturbances, drugs (especially anticholinergics), alcohol withdrawal, pain, constipation, neurological disorder, hypoxia, sleep deprivation, surgery, and environmental factors (Young & Inouye, 2007).

Delirium is an acute dysfunction of arousal and/or attentional brain networks. Since arousal and attention are the bases for higher cognitive functions, most cognitive functions are affected. Neurochemically, delirium is characterized by disturbances in acetylcholine, dopamine, norepinephrine, glutamate, gamma aminobutyric acid, and serotonin systems. Cytokines and blood-brain barrier abnormalities may also play a role (Alagiakrishnan & Wiens, 2004; Van Der Mast, 1998).

Treatments for delirium target the underlying cause(s), as well as the associated behavioral problems and neuropsychiatric symptoms. Modifiable risk factors or precipitants should be addressed (e.g., by treating the underlying medical condition,

withdrawing of possible offending medications, correcting sensory deficits by using hearing aids and eyeglasses). Behaviors that put an individual at risk should be managed by changing the environment (e.g., providing access to familiar people and objects, protecting the individual on a locked treatment unit when there is a risk of wandering) and through behavioral interventions (e.g., reorientation, de-escalation techniques), possibly in combination with medications. Neuropsychiatric symptoms (e.g., perceptual disturbances, agitation, aggression) are managed with antipsychotics, mood stabilizers, or antiepileptics. Benzodiazepines may be useful in treating withdrawal from alcohol.

See also **Complications.**

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KALOYAN TANEV

DELIRIUM TREMENS (DTS).

Delirium tremens (DTs) refers to the most severe form of the alcohol withdrawal syndrome, occurring with the abrupt cessation of, or reduction in, alcohol consumption in an individual who has been a heavy drinker for many years. It is associated with a significant mortality rate of an estimated 1 to 5 percent, which is likely higher (perhaps up to 15 percent) if untreated.

DTs usually begin at seventy-two to ninety-six hours after the cessation of drinking and usually last two to three days but can occasionally last considerably longer. Early treatment of withdrawal symptoms is thought to prevent the risk of developing DTs and its related mortality. Risk factors for DTs include infection, a history of epileptic seizures, tachycardia (rapid heart rate) upon admission to hospital, withdrawal symptoms with a blood alcohol concentration 1 g/L, and a prior history of DTs. Concurrent medical conditions such as infection, trauma, and liver failure may increase the mortality of DTs.

Symptoms of DTs include those typically seen in delirium, including disorientation, confusion, fluctuating levels of consciousness and attention, vivid hallucinations, delusions, agitation, and also include those found in alcohol withdrawal; fever, elevated blood pressure, rapid pulse, sweating, and tremor. Delirium is the hallmark and defining feature of DTs and differentiates the syndrome from uncomplicated alcohol withdrawal. The delirium may at times be preceded by a withdrawal seizure, although a seizure neither defines nor is its presence required to diagnose DTs, and not all patients that experience withdrawal seizures develop DTs. The treatment of DTs necessitates close monitoring in the hospital setting.

For patients in alcohol withdrawal but without DTs, as the severity of withdrawal increases, patients may experience transient mild hallucinations that are auditory, visual, or tactile in nature. Loss of insight into hallucinations or development of more severe and persistent hallucinations may suggest that the syndrome has progressed or is progressing to DTs. Delirium tremens is differentiated from the syndromes of *alcoholic hallucinosis* and *chronic alcoholic hallucinosis*, which are terms used inconsistently in the literature to refer to the transient hallucinosis experienced during alcohol withdrawal and/or the subsequent development of a state of psychosis accompanied by hallucinations and/or delusions (particularly persecutory) that persists beyond the period of detoxification. There is controversy as to whether chronic alcoholic hallucinosis syndrome exists.

See also **Delirium; Withdrawal.**

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DENMARK. *See* **Nordic Countries (Denmark, Finland, Iceland, Norway, and Sweden).**

DEPRESSION. The term *depression* refers to both a mood and a group of psychiatric disorders. In the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV-TR*, 2000) depressed mood occurs as part of major depressive disorder (MDD), dysthymic disorder (chronic, less severe depression), and schizoaffective disorder (psychosis co-occurring with depressed or manic mood), and can also occur in bipolar disorder (periods of mania that can alternate with periods of depression) and during intoxication or withdrawal from certain substances.

Many people experience brief periods of depressed mood that are often responses to stressful life events or negative experiences. However, when depression-related symptoms cluster, persist, and ultimately cause impairment in functioning, the person is considered to be experiencing a depressive syndrome. The *DSM-IV* classifies this syndrome as a major depressive episode and requires the following criteria: a period of low mood (or loss of interest or pleasure in usual activities) lasting at least two weeks; four or more out of eight additional symptoms (significant change in weight or appetite, poor or increased sleep nearly every day, psychomotor agitation or retardation that is noticeable to others nearly every day, fatigue or low energy nearly every day, feelings of worthlessness or inappropriate guilt nearly every day, difficulty concentrating or making decisions nearly every day, and recurring thoughts of death, suicide, or suicidal attempt); and functional impairment or clinically significant distress.

If the symptoms of depression are the direct physiological effects of heavy consumption of alcohol or another psychoactive substance and are greater than the expected effects of intoxication or withdrawal, the depression is considered to be substance-induced. In *DSM-IV*, normal bereavement is not present if inappropriate guilt, thoughts of death unrelated to the deceased person, a preoccupation with worthlessness, marked psychomotor retardation, and hallucinations that are not a phenomenon shared by others in one's cultural group are present, signaling the presence of a major depressive episode. Major depressive disorder is also distinguished from low mood resulting from a medical condition and mood changes that are due to exposure to a toxin or chemical substance.

Major Depression is one of the most common psychiatric disorders experienced by adults. One study of data drawn from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions indicated that approximately 13 percent of the U.S. population has experienced a major depressive episode (Hasin et al., 2005). Women have higher rates of lifetime depression than men (17.10 percent vs. 9.01 percent), Native Americans are at greater risk for depression than other ethnic groups, and individuals who are middle-aged or widowed, separated, or divorced, and those with lower income levels are at increased risk. Depression is associated with substantial impairment (Weissman et al., 1991; Kessler et al., 1994; Kessler et al., 2003), psychiatric comorbidity (Weissman et al., 1991; Kessler et al., 1994; Kessler et al., 2003; Hasin et al., 2005), poor health (Dentino et al., 1999), and mortality (Insel & Charney, 2003).

The cause of depression is multi-systemic. Imaging studies have shown abnormal neurochemical activity and changes in volume in specific areas of the brain of depressed people. These biological changes, combined with genetic and psychosocial factors (e.g., life events, learned behaviors, and cognitions) all interact to varying degrees. Depression is a highly recurrent but treatable illness. Effective treatment options are available (e.g., psychotherapy, pharmacotherapy, psychoeducation, and, generally as a last option, electroconvulsive therapy), and the

choice of treatment depends on multiple factors such as the individual's psychiatric history, the severity of the current episode, family and social support, general medical health, the patient's level of motivation, and the compatibility of the treatment with the patient's current circumstances.

See also **Complications: Mental Disorders; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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SHARON SAMET

DESIGNER DRUGS. "Designer drugs" are synthetic chemical analogs of abused substances that are designed to produce pharmacological effects similar to the substances they mimic. In the pharmaceutical industry, the design of new drugs often utilizes principles of basic chemistry, so that the structure of a drug molecule is slightly altered in order to change its pharmacological activity. This strategy has a long and successful history in medical pharmaceutics, and many useful new drugs or modifications of older drugs have clearly resulted in improved health care for many people throughout the world. The principles of structure-activity relationships have been applied to many medically approved drugs, especially in the search for a nonaddicting opioid analgesic for the treatment of pain. However, the clandestine production of "designer" street drugs is intended to avoid federal regulation and control. This practice can often result in the appearance of new and unknown substances with wide-ranging variations in purity. The quality of personnel involved in clandestine designer-drug synthesis can range from "cookbook" amateurs to highly skilled chemists, which means that these substances have the potential to cause dangerous toxicity with serious health consequences for the unwitting drug user.

A resurgence in the popularity of a relatively old drug, methamphetamine, was observed during the first decade of the twenty-first century. Although methamphetamine is manufactured in foreign or domestic "superlabs," the drug is also easily made in small clandestine laboratories with relatively inexpensive over-the-counter ingredients. This practice can lead to wide variations in the purity of the methamphetamine available for illicit distribution. Methamphetamine is a highly addictive central nervous system stimulant that was developed early in the twentieth century and initially used in nasal decongestants and bronchial inhalers. Like amphetamine, methamphetamine produces increased activity and talkativeness, anorexia, and a general sense of well-being. However, methamphetamine differs from amphetamine in that much higher levels of methamphetamine get into the brain when comparable doses are administered, making it a more potent stimulant drug. And while methamphetamine blocks the reuptake of dopamine at low doses, in a manner similar to cocaine, it also increases the release of dopamine, leading to much higher concentrations of this neurotransmitter. Although the pleasurable effects of methamphetamine most likely result from the release of dopamine, the elevated

release of this neurotransmitter also contributes to the drug's deleterious effects on nerve terminals. Specifically, brain-imaging studies have demonstrated alterations in the activity of the dopamine system that are due to methamphetamine use. Recent studies of chronic methamphetamine users have revealed structural and functional changes in areas of the brain associated with emotion and memory, which may account for many of the emotional and cognitive problems experienced by chronic users.

Addicts typically exhibit anxiety, confusion, insomnia, mood disturbances, and violent behavior, and they can also display a number of psychotic features, including paranoia, visual and auditory hallucinations, and delusions. These psychotic symptoms can last for months or years after methamphetamine use has ceased, and stress has been shown to precipitate the spontaneous recurrence of methamphetamine psychoses. Methamphetamine can also produce a variety of cardiovascular effects, including rapid heart rate, irregular heartbeat, and increased blood pressure. Hyperthermia (elevated body temperature) and convulsions may occur during a methamphetamine overdose, and, if not treated immediately, this can result in death. Tolerance to methamphetamine's pleasurable effects develops with chronic use, and abusers may take higher doses of the drug, take it more frequently, or change their method of drug intake in an effort to intensify the desired effects. Methamphetamine has also become associated with a culture of risky sexual behavior, both among men who have sex with men and heterosexual populations, because methamphetamine and related psychomotor stimulants can increase libido. Paradoxically, however, long-term methamphetamine abuse may be associated with decreased sexual functioning.

Other hallucinogenic designer drugs that are amphetamine analogs—such as methylenedioxyamphetamine (MDA), methylenedioxymethamphetamine (MDMA or "Ecstasy") and methylenedioxyethamphetamine (MDEA or "Eve")—can also produce acute and chronic toxicity. Acute toxicity from these drugs is usually manifested as restlessness, agitation, sweating, high blood pressure, tachycardia, and other cardiovascular effects, all of which are suggestive of excessive central nervous system stimulation. Following chronic administration, MDA produces a degeneration of serotonergic nerve terminals in rats, implying that it might induce chronic neurological damage in humans as well.

Newer designer drugs of abuse that have recently emerged on the black market include amphetamine-derived drugs such as para-methoxyamphetamine (PMA), para-methoxymethamphetamine (PMMA) and 4-methylthioamphetamine (4-MTA). In addition, newer designer drugs of the benzyl or phenyl piperazine type, and of the pyrrolidinophenone type, have gained popularity and notoriety as party or "rave" drugs. These include N-benzylpiperazine (BZP); 1-(3, 4-methylenedioxybenzyl)piperazine (MDBP); 1-(3-chlorophenyl)piperazine (mCPP); 1-(3-trifluoromethylphenyl)piperazine (TFMPP); 1-(4-methoxyphenyl)piperazine (MeOPP); alpha-pyrrolidinopropiophenone (PPP); 4'-methoxy-alpha-pyrrolidinopropiophenone (MOPPP); 3', 4'-methylenedioxy-alpha-pyrrolidinopropiophenone (MDPPP); 4'-methyl-alpha-pyrrolidinopropiophenone (MPPP); and 4'-methyl-alpha-pyrrolidinoexanophenone (MPHP). These drugs produce feelings of euphoria and energy and a desire to socialize. While "word on the street" suggests that these designer drugs are safe, studies in rats and primates have suggested that they present risks to humans. In fact, a variety of adverse effects have been associated with the use of this class of drugs in humans, including a life-threatening serotonin syndrome (due to an excess of this neurotransmitter), and toxic effects on the liver and brain that result in behavioral changes.

An opioid that has resulted in serious health hazards on the street is fentanyl (Sublimaze), a potent and extremely fast-acting narcotic analgesic with a high abuse liability. This drug has also served as a template for many look-alike drugs in the clandestine chemical laboratory. Very slight modifications in the chemical structure of fentanyl can result in analogs such as para-fluoro-, 3-methyl-, or alpha-methyl-fentanyl, with relative potencies that are 100, 900, and 1,100 times that of morphine, respectively. Unfortunately, a steady increase in deaths from drug overdoses associated with fentanyl-like designer drugs has been reported.

Designer drugs already on the street, such as methamphetamine and related stimulants, can produce significant brain damage following long-term use, and analogs of the opioid fentanyl can produce

fatal overdoses. Taken to the extreme, the widespread illicit manufacture and use of designer drugs with unknown toxicity could result in millions of people ingesting the drug before the toxic effects are known, potentially producing an epidemic of neurodegenerative disorders and fatalities.

See also **Controlled Substances Act of 1970; MDMA; MPTP.**

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DEXTROAMPHETAMINE. This is the *d*-isomer of amphetamine. It is classified as a psychomotor stimulant drug and is three to four times as potent as the *l*-isomer in eliciting central nervous system (CNS) excitatory effects. It is also more potent than the *l*-isomer in its anorectic (appetite suppressant) activity, but slightly less potent in its cardiovascular actions. It is prescribed in the treatment of narcolepsy and obesity, although care must be taken in such prescribing because of the substantial abuse liability.

High-dose chronic use of dextroamphetamine can lead to the development of a toxic psychosis as well as to other physiological and behavioral problems. This toxicity became a problem in the United States in the 1960s, when substantial amounts of the drug were being taken for nonmedical reasons. Although still abused by some, dextroamphetamine is no longer the stimulant of choice for most psychomotor stimulant abusers.

See also **Amphetamine Epidemics, International; Coca/Cocaine, International.**

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MARIAN W. FISCHMAN

DIAGNOSIS OF SUBSTANCE USE DISORDERS: DIAGNOSTIC CRITERIA. *Diagnosis* is the process of identifying and labeling specific disease conditions. The signs and symptoms used to classify a sick person as having a disease are called *diagnostic criteria*. Diagnostic criteria and classification systems are useful for making clinical decisions, estimating disease

prevalence, understanding the causes of disease, and facilitating scientific communication.

Diagnostic classification provides the treating clinician with a basis for retrieving information about a patient's probable symptoms, the likely course of an illness, and the biological or psychological processes that underlie the disorder. For example, the *Diagnostic and Statistical Manual* (*DSM*) of the American Psychiatric Association is a classification of mental disorders that provides the clinician with a systematic description of each disorder in terms of essential features, age of onset, probable course, predisposing factors, associated features, and differential diagnosis. Mental health professionals can use this system to diagnose substance use disorders in terms of the following categories: acute intoxication, abuse, dependence, withdrawal, delirium, and other disorders. In contrast to screening, diagnosis typically involves a broader evaluation of signs, symptoms, and laboratory data as these relate to the patient's illness. The purpose of diagnosis is to provide the clinician with a logical basis for planning treatment and estimating prognosis.

Another purpose of classification is the collection of statistical information on a national and international scale. The primary purpose of the *World Health Organization's International Classification of Diseases* (*ICD*), for example, is the enumeration of morbidity and mortality data for public health planning. In addition, a good classification will facilitate communication among scientists and provide the basic concepts needed for theory development. Both the *DSM* and *ICD* have also been used extensively to classify persons for scientific research. Classification thus provides a common frame of reference in communicating scientific findings.

Diagnosis may also serve a variety of administrative purposes. When a patient is suspected of having a substance use disorder, diagnostic procedures are needed to exclude "false positives" (i.e., people who appear to have the disorder but who really do not) and borderline cases. Insurance reimbursement for medical treatment increasingly demands that a formal diagnosis be confirmed according to standard procedures or criteria. The need for uniform reporting of statistical data, as well as the generation of prevalence estimates for epidemiological research, often requires a diagnostic classification of the patient.

CLASSIFICATION SYSTEMS

Alcoholism and drug addiction have been variously defined as medical diseases, mental disorders, social problems, and behavioral conditions. In some cases, they are considered the symptom of an underlying mental disorder (Babor, 1992). Some of these definitions permit the classification of alcoholism and drug dependence within standard nomenclatures such as the *DSM* and *ICD*. The most recent revisions of both of these diagnostic systems—*DSM-IV* (1994) and *ICD-10* (1992)—have resulted in a high degree of compatibility between the classification criteria used in the United States and those used internationally. Both systems now diagnose dependence according to the elements first proposed by Edwards and Gross (1976). They also include a residual category (harmful alcohol use [*ICD-10*]; alcohol abuse [*DSM-IV*]) that allows classification of psychological, social, and medical consequences directly related to substance use.

HISTORY TAKING

Obtaining accurate information from patients with alcohol and drug problems is often difficult because of the stigma associated with substance abuse and the fear of legal consequences. At times, these individuals want help for the medical complications of substance use (such as injuries or depression) but are ambivalent about giving up alcohol or drug use entirely. It is often the case that these patients are evasive and attempt to conceal or minimize the extent of their alcohol or drug use. Acquiring accurate information about the presence, severity, duration, and effects of alcohol and drug use therefore requires a considerable amount of clinical skill.

The medical model for history taking is the most widely used approach to diagnostic evaluation. This model consists of identifying the chief complaint, evaluating the present illness, reviewing past history, conducting a review of biological systems (e.g., gastrointestinal, cardiovascular), asking about family history of similar disorders, and discussing the patient's psychological and social functioning. A history of the present illness begins with questions on the use of alcohol, drugs, and tobacco. The questions should cover prescription drugs as well as illicit drugs, with additional elaboration of the kinds of drugs, the amount used, and

the mode of administration (e.g., smoking, injection). Questions about alcohol use should refer specifically to the amount and frequency of using the major beverage types (wine, spirits, and beer). A thorough physical examination is important because each substance has specific pathological effects on certain organs and body systems. For example, alcohol commonly affects the liver, stomach, cardiovascular system, and nervous system, while drugs often produce abnormalities in "vital signs" such as temperature, pulse, and blood pressure.

A mental status examination frequently gives evidence of substance use disorders, which can be signaled by poor personal hygiene, inappropriate affect (e.g., sad, euphoric, irritable, anxious), illogical or delusional thought processes, and memory problems. The physical examination can be supplemented by laboratory tests, which sometimes aid in early diagnosis before severe or irreversible damage has taken place. Laboratory tests are useful in two ways: (1) alcohol and drugs can be measured directly in blood, urine, or exhaled air; (2) biochemical and psychological functions known to be affected by substance use can be assessed. Many drugs can be detected in the urine for 12 to 48 hours after their consumption. An estimate of blood alcohol concentration (BAC) can be made directly by blood test or indirectly by means of a breath or saliva test. Elevations of the liver enzyme gamma-glutamyl transpeptidase (GGTP) or the protein carbohydrate-deficient transferrin (CDT) are sensitive indicators of chronic and heavy alcohol intake. However, while these tests can detect recent use of a wide variety of psychoactive substances (e.g., opioids, cannabis, stimulants, barbiturates), they are not able to detect alcohol or drug dependence.

In addition to the physical examination and laboratory tests, a variety of diagnostic interview procedures have been developed to provide objective, empirically based, reliable diagnoses of substance use disorders in various clinical populations. One type, exemplified by the Diagnostic Interview Schedule (DIS; see Robins et al., 1981) and the Composite International Diagnostic Interview (CIDI; see Robins et al., 1988), is highly structured and requires a minimum of clinical judgment by the interviewer. These interviews provide information not only about substance use disorders, but also about physical conditions and psychiatric disorders that are commonly associated with substance abuse. Because of its standardized questioning procedures, the CIDI has been used by the World Health Organization to estimate the prevalence of mental disorders, including substance use disorders, in the general populations of countries throughout the world (Haro et al., 2006). In the United States, the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) has been used extensively in population surveys, including the National Epidemiologic Survey on Alcohol and Related Conditions (Grant et al., 2003). It covers alcohol consumption, tobacco use, family history of depression, and selected *DSM-IV* Axis I and II psychiatric disorders.

A second type of diagnostic interview is exemplified by the Structured Clinical Interview for *DSM-IV* (SCID), which is designed for use by mental health professionals (Spitzer et al., 1992; First et al., 2002). The SCID assesses the most commonly occurring psychiatric disorders described in *DSM-IV*, including mood disorders, schizophrenia, and substance use disorders. A similar clinical interview designed for international use is the Schedules for Clinical Assessment in Neuropsychiatry (SCAN; see Wing et al., 1990). The SCID and SCAN interviews allow the experienced clinician to tailor questions to fit the patient's understanding, to ask additional questions that clarify ambiguities, to challenge inconsistencies, and to make clinical judgments about the seriousness of symptoms. Both are modeled on the standard medical history practiced by many mental health professionals. Questions about the chief complaint, past episodes of psychiatric disturbance, treatment history, and current functioning all contribute to a thorough and orderly psychiatric history that is extremely useful for diagnosing substance use disorders. The Psychiatric Research Interview for Substance and Mental Disorders (PRISM; Hasin et al., 2006) is another semistructured diagnostic interview. It is designed to deal with the problems of psychiatric diagnosis when subjects or patients drink heavily or use drugs. The PRISM is used for making a number of *DSM-IV* Axis I and Axis II diagnoses, including alcohol and drug use disorders, in a way that allows differentiation of psychiatric disorders from substance-induced disorders and from the expected effects of intoxication and withdrawal.

In recent years, there has been interest in developing better methods to obtain accurate information from patients with substance use disorders, both for diagnostic purposes and for the measurement of treatment outcomes. It has been assumed that information obtained from alcohol and drug users cannot be trusted, because they often unconsciously deny that they have a problem or deliberately lie about their substance use to avoid the embarrassment of being labeled as an alcoholic or a drug addict. Another factor is clinical suspicion that individuals with substance use disorders often are not capable of reporting their symptoms accurately, due to the cognitive effects of chronic substance use.

With advances in the technology of psychiatric interviewing, questionnaire design, and psychological measurement, it is now possible to obtain valid measurement at the symptom level and to improve classification accuracy at the syndrome level (Haro et al., 2006). According to one systematic review of methodological studies, self-report measures using questionnaires and interviews tend to be valid and reliable in the aggregate under most circumstances (Del Boca & Noll, 2000). Nevertheless, patients may bias their responses in a socially desirable direction when they do not understand the purpose of the questions, feel threatened by the possible outcome of the diagnostic evaluation (e.g., being labeled as having a psychiatric disorder), have cognitive disabilities that affect memory and recall, or have personality characteristics (e.g., psychopathy) that increase the chances of deliberate lying.

DIAGNOSIS OF ABUSE AND HARMFUL USE

A major diagnostic category that has received increasing attention in research and clinical practice is substance abuse—in contrast to dependence. This category permits the classification of maladaptive patterns of alcohol or drug use that do not meet criteria for dependence. The diagnosis of abuse is designed primarily for persons who have recently begun to experience alcohol or drug problems, as well as for chronic users whose substance-related consequences develop in the absence of marked dependence symptoms. Examples of situations in which this category would be appropriate include: (1) a pregnant woman who keeps drinking alcohol even though her physician has told her that it could cause fetal damage; (2) a college student whose weekend binges result in missed classes, poor grades, and alcohol-related traffic accidents; (3) a middle-aged beer drinker regularly consuming a six-pack each day who develops high blood pressure and fatty liver in the absence of alcohol-dependence symptoms; and (4) an occasional marijuana smoker who has an accidental injury while intoxicated.

In the fourth revision of the *Diagnostic and Statistical Manual* (American Psychiatric Association, 1994), *substance abuse* is defined as a maladaptive pattern of alcohol or drug use leading to clinically significant impairment or distress, as manifested by one or more of the symptoms listed in Table 1. (For comparative purposes, the table also lists the criteria for harmful use in *ICD-10*.) To assure that the diagnosis is based on clinically meaningful symptoms, rather than the results of an occasional excess, the duration criterion specifies how long the symptoms must be present to qualify for a diagnosis.

In *ICD-10*, the term *harmful use* refers to a pattern of using one or more psychoactive substances that causes damage to health. The damage may be: (1) physical (physiological)—such as pancreatitis from alcohol or hepatitis from needle-injected drugs; or (2) mental (psychological)—such as depression related to heavy drinking or drug use. Adverse social consequences often accompany substance use, but they are not in themselves sufficient to result in a diagnosis of harmful use. The key issue in the definition of this term is the distinction between perceptions of adverse effects (e.g., wife complaining about husband's drinking) and actual health consequences (e.g., trauma due to accidents during drug intoxication). Since the purpose of *ICD* is to classify diseases, injuries, and causes of death, *harmful use* is defined as a pattern of use already causing damage to health.

Harmful patterns of use are often criticized by others, and they are sometimes legally prohibited by governments. However, the fact that alcohol or drug intoxication is disapproved by another person or by the user's culture is not in itself evidence of harmful use, unless socially negative consequences have actually occurred at dosage levels that also result in psychological and physical consequences. This is the major difference that distinguishes

	ICD-10 Criteria for Harmful Use	DSM-IV Criteria for Abuse
Symptom Criteria	Clear evidence that alcohol or drug use is responsible for causing actual psychological or physical harm to the user	A maladaptive pattern of alcohol or drug use indicated by at least one of the following: (1) failure to fulfill major role obligations at work, school, or home (e.g., neglect of children or household); (2) use in situations in which it is physically hazardous (e.g., driving an automobile); (3) recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct); (4) continued substance use despite having recurrent social or interpersonal problems
Duration Criterion	The pattern of use has persisted for at least 1 month or has occurred repeatedly over the previous 12 months	One or more symptoms has occurred during the same 12-month period

Table 1. Diagnostic Criteria for Harmful Use (IDC-10) and Substance Abuse (DSM-III-R, DSM-IV). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

ICD-10's harmful use from *DSM-IV*'s substance abuse—the latter category includes social consequences in the diagnosis of abuse.

THE DEPENDENCE SYNDROME CONCEPT

The diagnosis of substance use disorders in *ICD-10* and *DSM-IV* is based on the concept of a "dependence syndrome," which is distinguished from disabilities caused by substance use (Edwards, Arif, & Hodgson, 1981). An important diagnostic issue is the extent to which dependence is sufficiently distinct from abuse or harmful use to be considered a separate condition. In *DSM-IV*, *substance abuse* is a residual category that allows the clinician to classify clinically meaningful aspects of a patient's behavior when that behavior is not clearly associated with a dependence syndrome. In *ICD-10*, *harmful substance use* implies identifiable substance-induced medical or psychiatric consequences that occur in the absence of a dependence syndrome. In both classification systems, dependence is conceived as an underlying condition that has much greater clinical significance because of its implications for understanding etiology, predicting course, and planning treatment.

The dependence syndrome is seen as an interrelated cluster of cognitive, behavioral, and physiological symptoms. Table 2 summarizes the criteria used to diagnose dependence in *ICD-10* and *DSM-IV*. A diagnosis of dependence in all systems is made if three or more of the criteria have been experienced at some time in the previous twelve months.

The dependence syndrome may be present for a specific substance (e.g., tobacco, alcohol, or diazepam), for a class of substances (e.g., opioid drugs), or for a wider range of various substances. A diagnosis of dependence does not necessarily imply the presence of physical, psychological, or social consequences, although some form of harm is usually present. There are some differences among these classification systems, but the criteria are very similar, making it unlikely that a patient diagnosed in one system would be diagnosed differently in the other.

The syndrome concept implicit in the diagnosis of alcohol and drug dependence in *ICD* and *DSM* is a way of describing the nature and severity of addiction (Babor, 1992). Table 2 describes four dependence syndrome elements (salience, impaired control, tolerance, withdrawal, and withdrawal relief) in relation to the criteria for *DSM-IV*, and *ICD-10*. The same elements apply to the diagnosis of dependence on all psychoactive substances, including alcohol, marijuana, opioids, cocaine, sedatives, phencyclidine, other hallucinogens, and tobacco. The elements represent biological, psychological (cognitive), and behavioral processes. This helps to explain the linkages and interrelationships that account for the coherence of signs and symptoms. The co-occurrence of signs and symptoms is the essential feature of a syndrome. If three or more criteria occur repeatedly during the same period, it is likely that dependence is responsible for the amount, frequency, and pattern of the person's substance use.

Salience. *Salience* means that drinking or drug use is given a higher priority than other activities in spite of its negative consequences. This is reflected in the emergence of substance use as the preferred activity from a set of available alternative activities. In addition, the individual does not respond well to the

Dependence element	Diagnostic level	ICD-10 symptoms	DSM-IV symptoms
Salience	Cognitive, behavioral	Progressive neglect of alternative activities in favor of substance use	Important social, occupational, or recreational activities given up
	Behavioral	Persistence with substance use despite harmful consequences	Continued use despite psychological or physical problems
Impaired control	Behavioral, cognitive	A strong desire or sense of compulsion to drink or use drugs	
	Behavioral	Evidence of impaired capacity to control substance use in terms of its onset, termination, or levels of use	Substance often taken in larger amounts or over a longer period than intended Any unsuccessful effort or a persistent desire to cut down or control substance use
Tolerance	Biological, behavioral	Increased doses of substance are required to achieve effects originally produced by lower doses	Either (a) increased amounts needed to achieve desired effect; or (b) markedly diminished effect with continued use
Withdrawal and withdrawal relief	Behavioral, biological, cognitive	A physiological withdrawal state Use to relieve or avoid withdrawal symptoms and subjective awareness that this strategy is effective	Either (a) characteristic withdrawal syndrome for substance; or (b) the same substance taken to relieve or avoid symptoms

Table 2. ICD and DSM Diagnostic Criteria for Dependence (labeled according to diagnostic level—physiological, cognitive, and behavioral—and underlying dependence elements). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

normal processes of social control. For example, when drinking to intoxication goes against the tacit social rules governing the time, place, or amount typically expected by the user's family or friends, this may indicate increased salience.

One indication of salience is the amount of time or effort devoted to obtaining, using, or recovering from substance use. For example, people who spend a great deal of time at parties, bars, or business lunches give evidence of the increased salience of drinking over nondrinking activities.

Chronic drinking and drug intoxication interfere with the person's ability to conform to tacit social rules governing daily activities—such as keeping appointments, caring for children, or performing a job properly—that are typically expected by the person's reference group. Substance use also results in mental and medical consequences. Thus, a key aspect of the dependence syndrome is the persistence of substance use in spite of social, psychological, or physical harm—such as loss of employment, marital problems, depressive symptoms, accidents, and liver disease. This indicates that substance use is given a higher priority than other activities, in spite of its negative consequences.

One explanation for the salience of drug- and alcohol-seeking behaviors despite negative consequences is the relative reinforcement value of immediate and long-term consequences. For many alcoholics and drug abusers, the immediate positive reinforcing effects of the substance, such as euphoria or stimulation, far outweigh any delayed negative consequences, which may occur either infrequently or inconsistently.

Impaired Control. The main characteristic of impaired control is the lack of success in limiting the amount or frequency of substance use. For example, the alcoholic wants to stop drinking, but repeated attempts to do so have been unsuccessful. Typically, rules and other stratagems are used to avoid alcohol entirely or to limit the frequency of drinking. A resumption of heavy drinking after receiving professional help for a drinking problem is evidence of lack of success. The symptom is considered present if the drinker has repeatedly failed to abstain or has only been able to control drinking with the help of treatment, mutual-help groups, or removal to a controlled environment (e.g., prison).

In addition to an inability to abstain, impaired control is also reflected in the failure to regulate the amount of alcohol or drug consumed on a given occasion. The cocaine addict vows to snort only a small amount but then continues until the entire supply is used up. For the alcoholic, impaired control includes an inability to prevent the spontaneous onset of drinking bouts, as well as a failure to stop

Symptom	Alcohol	Amphetamine	Caffeine	Cocaine	Opioids	Nicotine
Craving					X	X
Tremor	X					
Sweating, fever	X				X	
Nausea or vomiting	X				X	
Malaise, fatigue	X	X		X		
Hyperactivity, restlessness	X	X	X	X		X
Headache	X					
Insomnia	X	X	X		X	
Hallucinations	X					
Convulsions	X					
Delirium	X					
Irritability	X	X		X		X
Anxiety	X		X	X		X
Depression	X			X		
Difficulty concentrating						X
Gastrointestinal disturbance			X			
Increased appetite						X
Diarrhea					X	

Table 3. Withdrawal symptoms associated with different psychoactive substances. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

drinking before intoxication. This behavior should be distinguished from situations in which the drinker's "control" over the onset or amount of drinking is regulated by social or cultural factors, such as during college beer parties or fiesta drinking occasions. One way to judge the degree of impaired control is to determine whether the drinker or drug user has made repeated attempts to limit the quantity of substance use by making rules or imposing limits on his or her access to alcohol or drugs. The more these attempts have failed, the more the impaired control is present.

Tolerance. *Tolerance* is a decrease in response to a psychoactive substance that occurs with continued use. For example, increased doses of heroin are required to achieve effects originally produced by lower doses. Tolerance may be physical, behavioral, or psychological. Physical tolerance is a change in cellular functioning. The effects of a dependence-producing substance are reduced, even though the cells normally affected by the substance are subjected to the same concentration. A clear example is the finding that alcoholics can drink amounts of alcohol (e.g., a quart of vodka) that would be sufficient to incapacitate or kill nontolerant drinkers.

Tolerance may also develop at the psychological and behavioral levels, independent of the biological adaptation that takes place. Psychological tolerance occurs when a marijuana smoker or heroin user no longer experiences a "high" after the initial dose of the substance. Behavioral tolerance is a change in the effect of a substance because the person has learned to compensate for the impairment caused by a substance. Some alcoholics, for example, can operate machinery at moderate doses of alcohol without impairment.

Withdrawal Signs and Symptoms. A "withdrawal state" is a group of symptoms occurring after cessation of substance use. It usually occurs after repeated, and usually prolonged, drinking or drug use. Both the onset of and course of withdrawal symptoms are related to the type of substance and the dose being used immediately prior to abstinence. Table 3 lists some common withdrawal symptoms associated with different psychoactive substances. Some drugs, such as hallucinogens, do not typically produce a withdrawal syndrome after cessation of use. Although generally thought of as not being characterized by withdrawal symptoms, recent evidence supports the

existence of a cannabis (marijuana) withdrawal syndrome (Agrawal et al., 2008).

Alcohol withdrawal symptoms follow within hours of the cessation or reduction of prolonged heavy drinking. These symptoms include tremor, hyperactive reflexes, rapid heartbeat, hypertension, general malaise, nausea, and vomiting. Seizures and convulsions may occur, particularly in people with a preexisting seizure disorder. Patients may have hallucinations, illusions, or vivid nightmares, and sleep is usually disturbed. In addition to physical withdrawal symptoms, anxiety and depression are also common. Some chronic drinkers never have a long enough period of abstinence to permit withdrawal to occur.

The use of a substance with the intention of relieving withdrawal symptoms and with awareness that this strategy is effective are cardinal symptoms of dependence. Morning drinking to relieve nausea or the "shakes" is one of the most common manifestations of physical dependence in alcoholics.

Other Features of Dependence. To be labeled dependence, symptoms must have persisted for at least one month or must have occurred repeatedly (two or more times) over a longer period of time. The patient does not need to be using the substance continually to have recurrent or persistent problems. Some symptoms (e.g., craving) may occur repeatedly whether the person is using the substance or not.

Many patients with a history of dependence experience a rapid reinstatement of the syndrome following resumption of substance use after a period of abstinence. Rapid reinstatement is a powerful diagnostic indicator of dependence. It points to the impairment of control over substance use, the rapid development of tolerance, and frequently, physical withdrawal symptoms.

Patients who receive opiates or other drugs for pain relief following surgery (or for a malignant disease such as cancer) sometimes show signs of a withdrawal state when the use of these drugs is terminated. The great majority of these individuals have no desire to continue taking such drugs, and they therefore do not fulfill the criteria for dependence. The presence of a physical withdrawal syndrome in these patients does not necessarily indicate dependence, but rather a state of neuroadaptation to the drug that was being administered. It is commonly assumed that severe dependence is not reversible, and this assumption is supported by the rapid reinstatement of dependence symptoms when drinking or drug use is resumed after a period of detoxification.

CATEGORICAL VERSUS DIMENSIONAL APPROACHES TO DIAGNOSIS

Clinical decision-making often requires the classification of a patient's condition into discrete categories reflecting whether a disorder such as alcohol dependence is present or absent. This kind of categorical thinking is convenient for the diagnostician and consistent with the way in which physical diseases are diagnosed, but it may not fit the way in which substance use disorders are manifested in clinical practice. Typically, people with substance use disorders vary widely in the severity of their symptoms, with no clear demarcation between mild, moderate, and severe cases. This makes it difficult to diagnose patients whose problems with substance use are at the threshold between mild and moderate severity. For this reason, it has been proposed that the fifth revision of the *Diagnostic and Statistical Manual* (*DSM-V*) include the option of rating patients' substance use disorders along a continuum that reflects the actual severity of their dependence or abuse (Helzer et al., 2006). The concept of a continuum of alcohol dependence with various levels of severity is consistent with the original formulation of the dependence syndrome (Edwards et al., 1981), and it has been supported empirically by psychometric studies (Hasin, Liu, et al., 2006).

MAKING A DISTINCTION BETWEEN ABUSE AND DEPENDENCE

Questions have been raised about whether two diagnoses are needed for substance use disorders, or whether one diagnosis that combines abuse and dependence criteria in some form could be more efficient while still being reliable and valid. A number of studies using factor analysis have shown that two factors are generally found to fit existing data better than a single factor, but that the two factors are very

highly correlated (Hasin, Hatzenbuehler, et al., 2006). In the first decade of the twenty-first century, investigators have used Item Response Theory (IRT) analysis to examine alcohol abuse and dependence criteria in general population data (Saha et al., 2006). These investigators found that alcohol abuse and dependence criteria appear to combine well into a single continuum of severity, with some abuse criteria (e.g., interpersonal problems related to drinking, failure to perform in major roles) actually indicating more severe aspects of dependence than some of the currently used dependence criteria (e.g., drinking more or longer than intended). However, whether these findings will extend to other substances remains a question to be answered by further research.

See also **Addiction: Concepts and Definitions; Alcoholism: Origin of the Term; Blood Alcohol Concentration; Computerized Diagnostic Interview Schedule for DSM-IV (C DIS-IV); Diagnostic and Statistical Manual (DSM); International Classification of Diseases (ICD); Models of Alcoholism and Drug Abuse; Physical Dependence; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Structured Clinical Interview for DSM-IV (SCID); Tolerance and Physical Dependence; Wikler's Conditioning Theory of Drug Addiction.**

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THOMAS F. BABOR

DIAGNOSTIC AND STATISTICAL MANUAL (DSM).

The *Diagnostic and Statistical Manual of Mental Disorders (DSM)* is the most widely accepted psychiatric diagnostic system in the United States, although psychiatric disorders are also included in the *International Classification of Diseases* (*ICD*). First published by the American Psychiatric Association (APA) in 1952, the *DSM* is used by medical professionals, insurance companies, the pharmaceutical industry, and the court system to diagnose and define mental illnesses and disorders, including substance abuse and dependence. In fact, the diagnosis code assigned to a case often determines insurance reimbursement for treatment. The book is also an important indicator of societal mores: Until 1973 homosexuality was defined as a mental disorder. This suggests that at least some psychiatric disorders are experienced because of the way in which a society reacts to an individual's behavior, and what is considered deviant in some cultures may be normative in others.

The first tabulation of mental illness in the United States appeared in the 1840 census, when the categories *idiots* and *insane* were first counted. By the 1880 census seven types of mental illness were recognized, including epilepsy. In 1917 the American Medico-Psychological Association (now the APA), in conjunction with the National Commission on Mental Hygiene, further enlarged its categories of mental illness. This broader list, while certainly of greater clinical use, was still chiefly designed to count the numbers and types of patients in mental hospitals. Several years after this tabulation, the newly renamed APA released a compendium of nationally recognized psychiatric terms—most of which applied to psychotic disorders and severe neurological impairments—that would become part of the American Medical Association's standard classified nomenclature of disease.

After the end of World War II, the Veterans Administration (VA) added many more diagnoses to the APA inventory, incorporating the various psychological disorders exhibited by servicemen. This expanded compilation proved to be influential, for shortly after its publication, the World Health Organization (WHO) published the sixth edition of its *ICD*, which for the first time included information on mental disorders, much of it based on the VA classifications.

The first edition of the *DSM* (*DSM-I*) was little more than a pamphlet where symptoms were not specified in detail. Its importance, however, lay in its description and definition of the approximately 100 diagnostic categories then recognized by clinicians. The seventh and eighth editions of *ICD* heavily influenced *DSM-I*, like its successor, *DSM-II*. Until the publication of *DSM-III*, the American

system for classifying psychiatric disorders was virtually identical to the *ICD*.

During the 1970s, however, researchers affiliated with the Washington University School of Medicine (Feighner et al., 1972) developed the *research diagnostic* approach to psychiatric diagnosis, which emphasized clearly formulated and observable signs and symptoms that could be used for both research and clinical practice. *DSM-III*, published in 1980, incorporated this approach, adding clear diagnostic standards and objective descriptions of symptoms and behaviors.

DSM-III also introduced a multiaxial system for diagnostic evaluation to ensure that all relevant clinical information was considered. Axis I describes syndromes such as major depression, schizophrenia, and substance use disorders. Axis II covers childhood and personality disorders that often persist into adult life. Axis III refers to physical disorders or conditions that are potentially relevant to the understanding or management of the patient. Axis IV rates the severity of psychosocial stressors that have occurred in the year preceding the current evaluation and that may have contributed to the patient's symptoms. Axis V is a global assessment of psychological, social, and occupational functioning, which should be taken into account in treatment planning.

DEFINING SUBSTANCE USE DISORDERS

For the first time, *DSM-III* listed substance use disorders as a separate diagnostic category, distinguishing them from personality disorders, which they had previously been considered. In addition, the term "dependence" replaced the more generic terms "alcoholism" or "addiction," and was distinguished from *abuse* by the presence of the symptoms of tolerance or withdrawal. Alcohol and drug abuse were assigned to separate subcategories, permitting a greater differentiation and range of severity for each.

A revised version of *DSM-III* was published in 1987, containing important changes in the section on substance use disorders (Rounsaville, Spitzer, & Williams, 1986). One modification was the adoption of a new dependence syndrome concept (Edwards, Arif, & Hodgson, 1981), in which dependence was defined as an interrelated cluster of psychological symptoms: a strong desire or craving for the substance; physiological signs, especially tolerance and withdrawal; and behavioral indicators, in particular using the substance to relieve withdrawal discomfort. Significantly, the medical and social consequences of both acute intoxication and chronic substance use, such as accidents and liver damage, are not among the primary diagnostic criteria of dependence. They did, however, play a prominent role in defining the *substance abuse* category.

After the publication of the revised third edition in 1987 (*DSM-III-R*), a fourth edition (*DSM-IV*) was published in 1994, with a "Text Revision," known as the *DSM-IV-TR*, providing updated and revised information in 2000. *DSM-IV* contained further changes in the diagnosis of substance use disorders that were designed to assure compatibility between *DSM* and *ICD* (see Table 1). *DSM-IV* now defines substance dependence as a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by three or more of the following seven symptoms occurring in the same twelve-month period:

- *Tolerance*—the need for markedly increased amounts of the substance to achieve intoxication or the desired effect, or a markedly diminished effect with continued use of the same amount of the substance;
- *Withdrawal*—behavioral changes that occur when blood or tissue levels of the substance decline after a period of prolonged or heavy use; often accompanied by use of the substance to relieve withdrawal symptoms;
- *Impaired control*—taking the substance in larger amounts or over a longer period than was intended;
- *Unsuccessful attempts* (or a persistent desire) to cut down or control substance use;
- *Much time spent* in activities related to procuring or using the substance or recovering from its effects;
- *Giving up or reducing* important social, occupational, or recreational activities because of substance use;
- *Continued use* despite knowledge of persistent or recurrent physical or psychological problems caused or worsened by use of the substance.

In *DSM-IV*, patients can be diagnosed as dependent on any of the following: alcohol, tobacco, sedatives and hypnotics, anxiolytics, cannabis (marijuana), stimulants, opioids, cocaine, hallucinogens, PCP (phencyclidine), or a combination

ICD-10 Dependence Syndrome	DSM-IV Substance Dependence
A cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or a class of substances takes a higher priority for an individual than other behaviours that once had greater value. A central characteristic of the syndrome is the desire (often strong, sometimes overpowering) to take psychoactive drugs (medically prescribed or not), alcohol, or tobacco. There may be evidence that return to substance use after a period of abstinence leads to a more rapid reappearance of other features of the syndrome than occurs with nondependent individuals. *Diagnostic guidelines* A definite diagnosis of dependence should usually be made only if three or more of the following have been experienced or exhibited during the previous year: (a) a strong desire or sense of compulsion to take the substance; (b) difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use; (c) a physiological withdrawal state . . . when substance use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms; (d) evidence of tolerance, such that increased doses of the substance are required to achieve effects originally produced by lower doses (examples are alcohol- and opiate-dependent individuals who may take doses sufficient to incapacitate or kill nontolerant users); (e) progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects; (f) persisting with substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; determination should be made of the user's actual or expected awareness of the nature and extent of the harm Narrowing of the personal repertoire of patterns of psychoactive substance use has also been described as a characteristic feature (e.g., a tendency to drink alcoholic drinks in the same way on weekdays and weekends, regardless of social constraints that determine appropriate drinking behaviour).	A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three or more of the following occurring at any time in the same twelve-month period: (1) tolerance, as defined by either of the following: (a) need for markedly increased amounts of the substance to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of the substance (2) withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome for the substance . . . (b) the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms (3) the substance is often taken in larger amounts or over a longer period than was intended (4) a persistent desire or unsuccessful efforts to cut down or control substance use (5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects. (6) important social, occupational, or recreational activities given up or reduced because of substance use (7) continued substance use despite knowledge of having had a persistent or recurrent physical or psychological problem that was likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption) Specify if: *with physiological dependence:* Evidence of tolerance or withdrawal (i.e., either item [1] or [2] is present): *without physiological dependence:* No evidence of tolerance or withdrawal (i.e., neither item [1] nor [2] is present).

Table 1. A comparison of *ICD-10* and *DSM-IV* criteria for dependence. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

of drugs, which is known as polysubstance dependence. The most important factor in determining dependence, according to the *DSM-IV*, is not simply the abuse of alcohol or drugs, but the patient's inability to stop using the substance(s) despite recognizing the serious problems this causes (i.e., impaired control over substance use).

FUTURE VERSIONS

The fifth version of the *DSM* is currently in the planning stage, with publication of the new criteria tentatively scheduled for 2012. As with the previous two versions, the revision process leading to DSM-V will be guided by a task force responsible for conducting literature reviews, independent data analyses, field trials of the new criteria, consensus conferences, and the publication of background monographs. One such monograph (Saunders et al., 2007) contains papers written by an international group of experts that are designed to stimulate research on critical diagnostic issues related to substance use disorders. Among the issues under consideration in the next revision to DSM are addictions that do not require substance use (e.g., pathological gambling, Internet addiction), the need for graded or continuous measures rather than yes-or-no diagnoses, whether to diagnose abuse independently from dependence, and whether to drop the category of abuse entirely.

See also **Addiction: Concepts and Definitions; Alcoholism: Origin of the Term; Diagnosis of Substance Use Disorders: Diagnostic Criteria; Models of Alcoholism and Drug Abuse; Personality Disorders.**

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DIAGNOSTIC INTERVIEW FOR GENETIC STUDIES (DIGS).

The Diagnostic Interview for Genetic Studies (DIGS; Nurnberger et al., 1994) is a clinical interview developed by principal investigators in the National Institute of Mental Health (NIMH) Schizophrenia and Bipolar Disorder Genetics Initiatives and NIMH extramural program staff for the assessment and differential diagnosis of major mood and psychotic disorders and related "spectrum" conditions. It is a semi-structured interview designed for use by trained interviewers (ideally those with clinical experience). Training generally consists of observation of interviews done by experienced personnel followed by administration under observation by a clinical supervisor. This process continues until the supervisor certifies that the interviewer has mastered the skip-out pattern and has achieved sufficient expertise in follow-up questions to code accurately the critical sections for diagnosis. Major Axis I disorders are covered, and there are additional sections on demographics, medical history, self-injurious behavior, present symptoms, comorbidity, and the Axis II diagnosis of antisocial personality disorder. A graphic timeline is included for the documentation of the longitudinal course of illness. A narrative summary is prepared by the interviewer at the end of the session. The narrative summary should be 1 to 2 pages in length and should cover all positive diagnoses including relevant criterion items, pertinent negative diagnoses, and should include a summary of the interview venue and length, as well as a judgment regarding reliability. Administration may require several hours for a complicated case. As of 2008, 30 to 40 different groups were using this instrument; it had been translated into six languages and cited in 397 publications.

The DIGS has the following features: (a) diagnoses can be made in multiple systems that include the Research Diagnostic Criteria (RDC), the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III*, *DSM-III-R*, and *DSM-IV*), Feighner et al. criteria (Feighner et al., 1972), and the *International Classification of Diseases, 10th Revision* (*ICD-10*); (b) a detailed assessment is made of the longitudinal course of illness, with particular attention to the co-occurrence of substance abuse and psychotic and mood symptoms; (c) detailed sections are included to assess current and past occurrences of episodes of substance abuse or dependence; and (d) a detailed psychosis section is included to collect data that allow a careful distinction to be drawn among schizophrenia, schizoaffective disorder, and other psychotic conditions. DIGS assessments of self-reported mental disturbance are organized into several domains of psychopathology: somatization, major depression, mania/hypomania, dysthymia/depressive personality/hyperthymic personality, alcohol abuse or dependence, other drug abuse or dependence, psychosis, schizotypal personality features, suicidal behavior, anxiety disorders, eating disorder, pathological gambling, and antisocial personality disorder. The DIGS collects self-reported demographic and medical history data, and ratings are also made on the Global Assessment Scale (GAS: Endicott et al.,

1976) and the Scales for the Assessment of Positive and Negative Symptoms (SANS, SAPS: Andreasen et al., 1990). Schizotypal and other Axis II Cluster A personality features are assessed by using a modified version of the Schedule for Schizotypy (SIS; Kendler et al., 1989). This combination in the DIGS of features (including both lifetime diagnoses in multiple systems and current mood state assessment) is unique among structured interviews for psychiatric disorders.

The DIGS is used in conjunction with information from family interviews and medical records to permit a final best estimate diagnosis by experienced clinicians. Typically, all available information is reviewed independently by two clinicians. If there is disagreement between them, they discuss the case together to reach a consensus. If a consensus cannot be reached (about 2% of cases), a third clinician reviews all information including the existing best estimate sheets and acts as a tiebreaker.

The development of the DIGS proceeded in parallel with a similar development of the SSAGA (Semi-Structured Assessment for the Genetics of Alcoholism). Some investigators participated in both processes. As a consequence, the structure and wording of some sections is similar between the two instruments, particularly with regard to substance abuse and mood disorders sections. Nevertheless, it should be noted that the DIGS is intended to allow more flexible use and scoring by interviewers with clinical experience.

The DIGS requires significant clinical judgment and summarizes information in narrative form as well as in ratings. The polydiagnostic approach involves recording clinical information in sufficient detail to allow differing criteria for diagnosis. This feature was incorporated because it creates the broadest possible dataset. Since the pathophysiologic characteristics of bipolar disorder and schizophrenia are unknown, valid definitions for these diagnoses are ambiguous. The polydiagnostic interview ensures maximum comparability of the data collected with other datasets.

The DIGS provides more details regarding the phenomenology of mood disorders and schizophrenia than many other available instruments. This is an inevitable consequence of its polydiagnostic aspect, since each diagnostic system requires some items not found in others. Many items have been included expressly for gathering descriptive information not required by any current diagnostic scheme, but which permit the construction of quantitative phenotypes or reconfiguration of the information gathered into new biologically based categories. For example, questions regarding mixed states of mania and depression, rapid cycling, suicidal behavior and comorbidity are included, as well as a timeline to help specify the course of illness.

As part of interview development, a two-phase reliability study was conducted with three major goals: (a) to determine the reliability of key diagnoses; (b) to determine the feasibility of automated scoring of the DIGS using external diagnostic algorithms; and (c) to assess diagnostic reliability among collaborating sites. Six weeks of independent interviewing at each site (phase 1) was followed by two weeks of cross-site interviewing (phase 2). Since there were no significant site differences in overall agreement in either phase of the reliability study, data were combined within each phase for the analysis of individual diagnoses (bipolar disorder, unipolar depression, schizophrenia, and schizoaffective disorder). For all target diagnoses except schizoaffective disorder, values of kappa (a chance corrected measure of diagnostic agreement) obtained for algorithmic and interviewer clinical diagnoses were in the excellent range: 0.73 to 0.96. For the entire sample, agreement on algorithmic criteria defining specific syndrome patterns was high: for example, *DSM-III-R* major depressive episode criterion A: 87%, kappa=0.78; manic episode criteria A and B: 71%, kappa=0.72; and schizophrenia criterion A: 74%, kappa=0.77.

The DIGS 2.0 was used in Genetics Initiative family studies starting in 1990. Version 3.0/B of the DIGS was created in 1998 to allow additional distinctions among diagnoses and other clinical features and to provide compatibility with *DSM-IV*.

Version 4.0/BP of the DIGS was developed in 2003. As part of the collaborative effort during the last funding period, the DIGS was reviewed and revised (DIGS 4.0) to allow collection of additional data on post-traumatic stress disorder and adult attention deficit disorder. A major change was made in the Best Estimate Diagnostic process, to incorporate

clinician judgment of multiple phenotypic indicators including age of onset and number of episodes of depression, hypomania, and mania; temporal relationship of mood disorder to substance abuse and psychosis; evidence of mixed episodes and rapid cycling; and a summary of the family history information. All of these indicators are scored independently by a senior clinician (at most sites a psychiatrist) based on medical records and interview information.

The DIGS, version 4, is available as an electronic form for INFOTECH Soft's Aspect mental health assessment platform. Thus it may be administered by computer (e.g., by an interviewer using a laptop or tablet computer in the field), and the computerized version can later be used to support the best estimate process.

The DIGS is designed to be used along with the FIGS (Family Instrument for Genetic Studies), which allows a comprehensive assessment of a family pattern of illness. The FIGS begins with the construction of a pedigree, then moves to general screening questions: "Has any member of your family had psychiatric or emotional problems?", and finally asks about each first-degree relative in turn, including symptom assessment, treatment history, and impairment.

The DIGS and FIGS are both available through the NIMH Genetics Initiative Web site at zork.wustl.edu. This Web site also contains a manual for the 3.0/B version and a link to the data entry system for the 4.0 version. Additional information is available from the authors.

See also **Addictive Personality and Psychological Tests; Alcohol: Psychological Consequences of Chronic Abuse; Antisocial Personality Disorder; Computerized Diagnostic Interview Schedule for DSM-IV (C DIS-IV); Depression; International Classification of Diseases (ICD); Schizophrenia; Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA); Structured Clinical Interview for DSM-IV (SCID).**

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CAROLYN YORK O'NEIL

DIAGNOSTIC INTERVIEW SCHEDULE FOR DSM-IV.

See **Computerized Diagnostic Interview Schedule for DSM-IV (C DIS-IV).**

DIHYDROMORPHINE.

Dihydromorphine is a semisynthetic opioid analgesic (painkiller) derived from morphine. Structurally, it is very similar to morphine—the only difference being the reduction of the double bond between positions 7 and 8 in morphine to a single bond. Although slightly more potent than morphine in relieving pain, it is not widely used clinically. At standard analgesic doses, it has a side-effect profile very similar to that of morphine. These include constipation and respiratory depression. Chronic use will produce tolerance and physical dependence.

See also **Addiction: Concepts and Definitions; Opiates/Opioids; Opioid Complications and Withdrawal.**

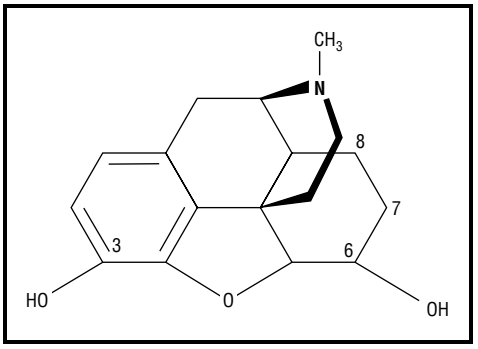

Figure 1. Chemical structure of dihydromorphine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

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GAVRIL W. PASTERNAK

DIMETHYLTRYPTAMINE (DMT). This drug is a member of the hallucinogenic substances known as indoleamines. These are compounds that are structurally similar to the neurotransmitter serotonin. Although found in certain plants and, according to some evidence, can be formed in the brain, DMT is synthesized for use. Its effects are similar to those produced by lysergic acid diethylamide (LSD), but unlike LSD, DMT is inactive after oral administration. It must be injected, sniffed, or smoked.

DMT has a rapid onset, usually within one minute, but the effects last for a much shorter period than those produced by LSD—with the user feeling "normal" within thirty to sixty minutes. This is because DMT is very rapidly destroyed by the enzyme monoamine oxidase, which metabolizes structurally related compounds, such as serotonin. The dose amount of DMT is critical, since larger doses produce slightly longer, much more intense, and sometimes very uncomfortable "trips" than do lower doses. The sudden and rapid onset of a period of altered perceptions that soon terminates is also disconcerting to some users. DMT was known briefly as the "businessman's LSD"—one could have a psychedelic experience during the lunch hour and be back at work in the afternoon. It has, however, in fact never been a widely available, steadily obtainable, or popular drug on the street.

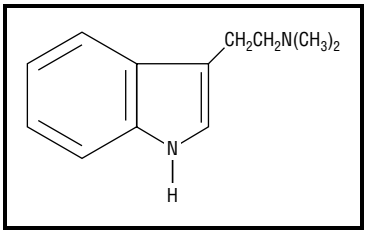

Figure 1. Chemical structure of dimethyltryptamine (DMT). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **DOM; MDMA.**

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DISTILLATION. Distillation is the process of purifying liquid compounds on the basis of different boiling points or the process of separating liquids from compounds that do not vaporize. Since the actual process causes liquids to precipitate in a wet mist or drops that concentrate and drip, the word derives from the Latin *de* (from, down, away) + *stillare* (to drip).

In the simplest form of distillation, saltwater can be purified to yield freshwater by steam distillation, leaving a residue of salt. Distillation is also the process by which alcohol (ethanol, also called ethyl alcohol) as liquors or spirits, are separated from fermenting mashes of grains, fruits, or vegetables. When this process is used to distill alcohol, it is based on the following: Ethyl alcohol (C_2H_6O) has a lower boiling point than does water (78.5°C versus 100°C), so alcohol vapors rise first

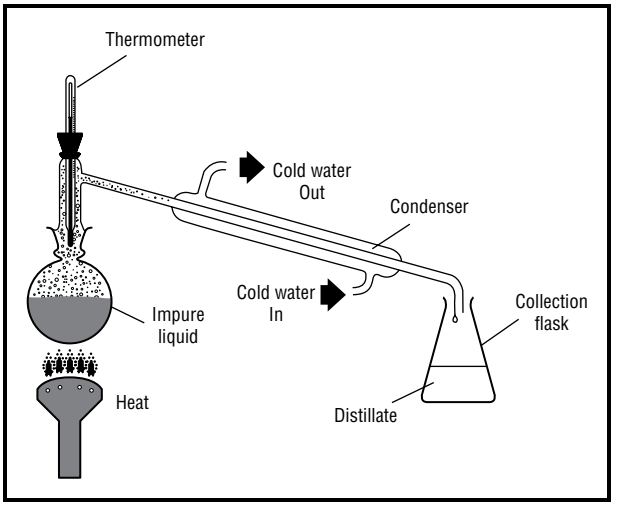

Figure 1. Simple distillation apparatus. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

into the condenser, where cool water circulates around the outside of the condenser, causing the alcohol vapors to return to liquid form and drop into the collection flask. The purity of the distillate can be increased by repeating the process several times.

About 800 CE, the process of distillation was evolved by the Arabian alchemist Jabir (or Geber) ibn Hayyah. He may also have named the distillate *alcohol*, since the word derives from an Arabic root, *al-kuhul*, which refers to powdered antimony (kohl) used as an eye cosmetic in the Mediterranean region; with time and use it came to mean any finely ground substance, then the "essence," and eventually, the essence of wine—its spirit, or alcohol. It came into English from Old Spanish, from the Arabic spoken by the Moors of the Iberian peninsula during their rule there (750–1492 CE).

See also **Beers and Brews; Distilled Spirits, Types of; Fermentation.**

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DISTILLED SPIRITS, TYPES OF.

Distilled spirits (or, simply, spirits or liquors) are the alcohol-containing fluids (ethanol, also called ethyl alcohol) obtained via distillation of fermented juices from plants. These juices include wines, distillates of which are termed brandies. The most commonly used plants are sugarcane, potatoes, sugar beets, corn, rye, rice, and barley; various fruits such as grapes, peaches, and apples are also used. Flavors may be added to provide distinctive character.

All distilled spirits begin as a colorless liquid, pure ethyl alcohol (as it was called by 1869)—C_2H_6O. This had been called *aqua vitae* (Latin, water of life) by medieval alchemists; today it is often called grain alcohol, and the amount contained in distilled spirits ranges from 30 to 100 percent (60 to 200 proof)—the rest being mainly water.

Examples of distilled spirits include brandy, whiskey, rum, gin, and vodka. Brandy was called *brandewijn* by the Dutch of the 1600s—burned, or distilled, wine. It was originally produced as a means of saving space on trade ships, to increase the value of a cargo. The intent was to add water to the condensate to turn it back into wine, but customers soon preferred the strong brandy to the acidic wines it replaced. Cognac is a special brandy produced in the district around the Charente river towns of Cognac and Jarnac, in France, where wine is usually distilled twice, then put into oak barrels to age. The spirits draw color and flavor (tannins)

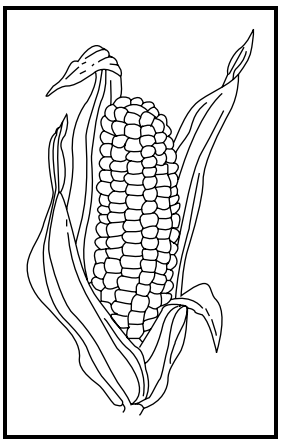

Figure 1. Corn. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

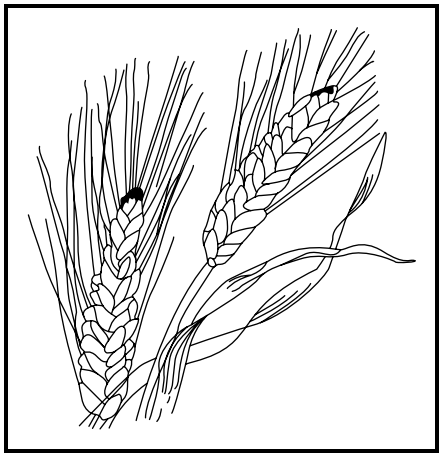

Figure 2. Wheat. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Figure 3. Oat. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

from the wood during the required five-year aging process.

Beer and wine were the most popular drinks of the New World colonists. By the mid-1700s, whiskey (from *uisce beathadh* in Irish Gaelic; *uisge beatha* in Scots Gaelic) was introduced into the American colonies by Scottish and Irish settlers to Pennsylvania. Whiskey is distilled off grains—usually corn or rye, but millet, sorghum, and barley are also used. Traditional American whiskeys are bourbons (named after Bourbon county in Kentucky), which are made from a sour mash of rye and corn. Bourbons typically contain 40 to 50 percent ethyl alcohol (called 80 to 100 proof, doubled by the liquor industry). Canadian whiskey is very similar to bourbon and to rye whiskey, while Irish whiskey is dry (has less sugar), with a distinctive austere flavor gained by filtration. All these whiskeys lack the smoky taste of Scotch whiskeys, which get their unique flavor by using malt that had been heated over peat fires. By using less malt and by aging for only a few years in used sherry casks (traditionally), a light flavor is produced; by using more malt and long aging, heavy peaty smoky flavors are produced. Today, some scotches and other whiskeys are blended to achieve uniform taste from batch to batch.

The distillation of fermented sugarcane (*Saccarum officinarum*) results in rum. Of all distilled spirits, rum best retains the natural taste of its base, because (1) the step of turning starch into sugar is unnecessary; (2) it can be distilled at a lower proof; (3) chemical treatment is minimized; and (4) maturing can be done with used casks. The amount of added (sugar-based) caramel gives rum its distinctive flavor and color—which can vary from clear to amber to mahogany. The New England colonists made rum from molasses, which is the thick syrup separated from raw sugar during crystal sugar manufacture. Caribbean colonists grew sugarcane and shipped barrels of molasses to New England. New Englanders shipped back barrels of rum. Both substances were originally ballast for the barrels, which were made from New England's local forests to hold the sugar shipped from the Caribbean to the mother country, England.

Gin is a clear distillate of a grain (or beer) base that is then reprocessed; juniper berries and other herbs are added to give it its traditional taste. Vodka is also clear liquor, often the same as gin without the juniper flavor. Traditional vodkas, made in Russia, Ukraine, Poland, and other Eastern European countries, are made from grain or potatoes at a very high proof; typical ranges are 65 to 95 proof, or about 33 to 43 percent ethyl alcohol. Vodka has no special taste or aroma, although some are slightly flavored with immersed grasses, herbs, flowers, or fruits. The Scandinavian aquavit is clear, like vodka, distilled from either grain or potatoes, and flavored with caraway seed; it is similar to Germany's kümmelvasser (*kümmel* means caraway in German). When any clear liquor is added to fruit syrups, the product is called a cordial or a liqueur. Swiss kirschwasser is, however, a clear high-proof cherry-based brandy (*kirsche* means cherry in German); and slivovitz is a clear high-proof Slavic plum-based brandy.

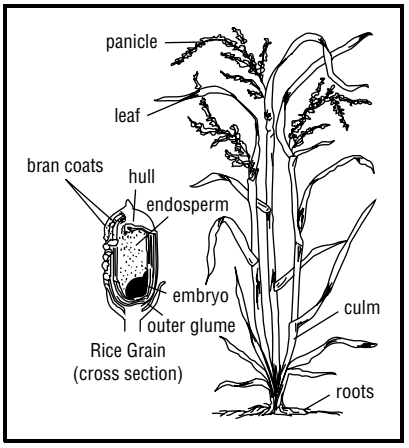

Figure 4. Rice. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

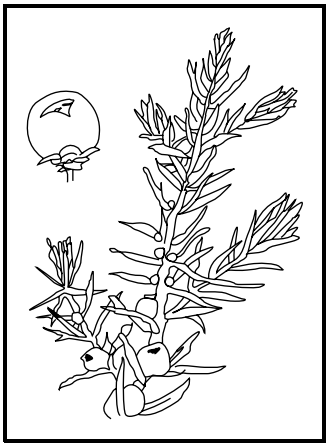

Figure 5. Juniper. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The raw grain alcohol distilled in the American South and in Appalachia has been called *white lightning* since the early 1900s; this is also known as moonshine, corn whiskey, or corn liquor—illegally produced in private nonlicensed stills, in very high proofs, to avoid state and federal controls or taxation. The term *firewater* was used along the American frontier after about 1815, to indicate any strong alcoholic beverage; this was often traded, given, or sold to Native Americans, causing cultural disruptions and social problems that continue even today. These include a high rate of alcoholism and children born with fetal alcohol syndrome.

See also **Alcohol: History of Drinking (International); Alcohol: History of Drinking in the United States; Beers and Brews.**

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SCOTT E. LUKAS

DISTILLED SPIRITS COUNCIL.

In 1974, the Distilled Spirits Council of the United States, Inc. (DISCUS) was formed by the merger of three organizations—the industrywide Licensed Beverage Industries, Inc. (LBI), the Distilled Spirits Institute (DSI), and the Bourbon Institute. DISCUS, headquartered in Washington, D.C., is supported by the distilled spirits producers, representing 90 percent of the liquor sold in the United States. In all major respects DISCUS is a trade association representing producers and marketers of distilled spirits sold in the United States.

DISCUS's primary functions are to maintain legislative relations with state and federal governments (lobbying); to conduct or support economic and statistical research; to promote export and standards of identity for American-made liquors; to maintain a voluntary code of advertising practices; and to represent the distilling industry on social issues of concern, such as teenage drinking, drunk driving, and other forms of alcohol abuse. State government relations activities are conducted by DISCUS regional representatives.

As a trade association, DISCUS seeks to inform the public about the importance of distilled spirits to the U.S. economy. By 1999, the distilled spirits industry generated $95 billion in U.S. economic activity annually and over 1.3 million people were employed in the United States through the manufacture, distribution, and sale of distilled spirits. Jobs within the distilled spirits industry account for more than $28 billion in U.S. wages.

As had its predecessor LBI, DISCUS has supported programs of alcohol abuse prevention and research conducted by independent groups and experts in education, traffic safety, and alcoholism. These projects have included the Grand Rapids,

Michigan, study of drunk driving (1961–1965) and the research led by Harburg and Gomburg (1978–1984) on how drinking may affect the offspring of different types of drinkers.

In addition to supporting the Harvard Medical School course for diagnosis and treatment of alcoholism, now adopted by eighty medical schools, DISCUS has provided extensive support to national organizations in the alcoholism field since 1970. Its approach is based on the knowledge that alcoholism is an identifiable illness and can respond to intervention and treatment.

In 1978, DISCUS endorsed the "responsible decisions on alcohol" approach developed by the Education Commission of the States, and in 1982, it supported the National Association of State Boards of Education in its nationwide project based on this concept (which includes abstinence). In 1980, DISCUS cooperated with the U.S. Department of Health and Human Services and other sponsors in supporting the Friends of the Family parenting education program.

In 1979, DISCUS became a charter member of the Licensed Beverage Information Council (LBIC), an industrywide consortium (beer, wine, and spirits at the producer, wholesaler, and retailer levels), whose membership includes nine other associations. LBIC has supported varied prevention groups and specialists in conducting medical and public education programs devoted to alcoholism as a treatable illness; fetal alcohol syndrome (FAS); teenage drinking; and drunk driving. The consortium has conducted the nationwide Friends Don't Let Friends Drive Drunk campaign.

DISCUS member companies are the principal supporters of the Century Council, a nonprofit organization dedicated to reducing alcohol abuse across the United States. Through public/private partnerships, Century Council investigates, funds, and implements innovative approaches to address the problems of drunk driving and underage drinking.

In 1994, DISCUS developed and initiated the Drunk Driving Prevention Act (DDPA), model legislation that strengthens drunk driving laws. Its provisions, many of which are being considered and adopted by state legislatures around the country, include mandatory alcohol and drug education for drivers; a ban of open containers in motor vehicles; Administrative License Revocation (ALR) authorizing a police officer to confiscate the license of any driver who either fails a chemical test or refuses to submit to it; zero tolerance for drivers under age 21; mandatory license revocation for persons under age 21 who attempt to purchase, consume, or misrepresent their age for the purpose of buying or consuming beverage alcohol; and mandatory alcohol and drug testing in fatal crashes.

DISCUS has also developed BACCHUS (Boosting Alcohol Consciousness Concerning Health of University Students). BACCHUS is a college-based peer education program to reduce alcohol abuse. Its educational materials include Open Doors, a Guide to Alcohol and Residence Life for Resident Administrators; Community College Guide to Peer Education; Gamma Guide (Greeks Advocating Mature Management of Alcohol); Certified Peer Educator Training Program; and Student Athletes as Peer Educators.

DISCUS has discouraged drinking by underage youth; encouraged adults who choose to drink to do so responsibly; and emphasized significant distinctions between normal social drinking and alcohol abuse.

The organization's economic research includes annual compilations of "apparent consumption" data (i.e., distilled spirits entering channels of trade) and an assessment of the liquor industry's contributions to the economy. Total U.S. distilled spirits consumption has declined in recent years, a fact noted by DISCUS as one of the many refutations of the "control of alcohol availability" hypothesis.

The DISCUS Code of Good Practice provides for self-regulation of advertising practices by distillers. An unusually high degree of compliance has been achieved even with nonmembers. The code was applied to radio in 1936, when that was a major medium; it has voluntarily excluded the use of television as an advertising medium by distillers since 1947. Contrary to a widely held impression, spirits advertising on television is not prohibited by law.

Distilled spirits have been the most heavily taxed consumer commodity in the United States. DISCUS and its predecessors have claimed over the years that such taxes are discriminatory and excessive, and they do not reduce chronic alcohol-abuse problems.

DISCUS has consistently argued that the tax structure imposed on distilled spirits is unjust because the government taxes spirits at a higher rate than beer and wine. It contends that standard servings of beer, wine, and distilled spirits contain the same amount of alcohol, yet the federal tax rate on distilled spirits is almost three times the rate on wine and over two times the rate on beer.

In 1999, DISCUS continued to lobby Congress for a reduction in excise taxes. DISCUS pointed out that more than half of the price that consumers spend on a typical bottle of distilled spirits is taxes. Federal, state, and local governments receive more than $18 billion per year in tax revenue from the beverage alcohol industry and tax revenues from the distilled spirits industry alone account for more than $7.5 billion. DISCUS pointed out that federal, state, and local governments combined realize fourteen times more in spirits tax revenues than the distillers make in profits. However, Congress has remained unresponsive to the attempt by DISCUS to reduce excise taxes.

As a long-standing policy, DISCUS and its members do not encourage people to start drinking or to drink too much. DISCUS's review of the research literature indicates that there is no scientific evidence that brand advertising either influences or shapes those behaviors. The marketing purpose of product advertising is to build consumer acceptance of specific brands, according to DISCUS. In the late 1990s, DISCUS began publicizing the health benefits of alcohol consumption. It noted a growing body of scientific evidence reporting that moderate beverage alcohol consumption may reduce the risk of cardiovascular disease, the leading cause of death in the United States. This potential benefit is equally available from moderate consumption of any form of beverage alcohol—distilled spirits, beer, or wine. However, DISCUS does not promote the use of alcohol consumption for health reasons.

See also **Alcohol: History of Drinking (International); Alcohol: History of Drinking in the United States; Legal Regulation of Drugs and Alcohol; Minimum Drinking Age Laws; Prevention; Social Costs of Alcohol and Drug Abuse; Tax Laws and Alcohol.**

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DOGS IN DRUG DETECTION. In 1970 the U.S. Customs Service faced a shrinking inspectional staff, a flood of illegal narcotics, and an increasing load of vehicles and passengers entering the United States. In that same year a manager in the U.S. Customs Service thought that dogs could be used to detect illegal narcotics. The manager's name has been lost in the corporate history of the Customs Service, yet years later dogs are not only used to detect narcotics, but U.S. Customs and Border Protection (CBP) canines also detect explosives, currency, agriculture (fruits, vegetables, and meats), and concealed persons. CBP canines are also used for BORSTAR (Border Patrol Search, Trauma, and Rescue). Dogs could be trained to detect anything that produces an odor. Although the idea of narcotic detector dogs originated in the U.S. Customs Service, Customs' managers had to go to the U.S. Air Force for the technical expertise—not in narcotic detection, because it did not exist, but dog training in general. The air force loaned the Customs Service five instructors to develop the program. Those instructors, using the age-old method of trial and error, developed a training method for narcotic detection that was still used in the 1990s. Through the years, several key aspects of the training program were identified and became the basis for a very successful program—dog selection, development of a conditioned response, and odor integrity.

It became evident that to make the training program successful the instructors had to start with a dog that displayed certain natural traits. Those traits were retrieval motivation and self-confidence. The instructors soon realized that a dog displaying a natural desire to retrieve was the easiest to condition for response to the narcotic odor. They used

A narcotics detector dog, inspecting student lockers. AP IMAGES.

the retrieval method just as the Russian physiologist Ivan Pavlov (1849–1936) used a bell: In Pavlov's experiments, he had observed that dogs salivate when food is placed in their mouths. He would give the dogs food while providing another stimulus such as a bell ringing. After a few repetitions, the dogs would salivate when they heard the bell ring—even without the food being present. The dogs had learned to associate the bell ringing with food. This response was called a *conditioned response*.

The Customs' instructors used a similar method to create a conditioned response to a drug odor. A dog was subjected to a series of retrieval exercises using a specific drug's odor. After each retrieval, the dog played a game of tug-of-war with its handler and received physical praise. The dog soon associated the specific drug odor with the game and the physical praise.

Using a dog's natural desire to retrieve as a selection criterion limited the number of breeds that could be considered for this type of training. It was obvious that most of the sporting breeds fit this criterion—golden retrievers, Labrador retrievers, German shorthair retrievers, and mixed breeds of these types. They have had the retrieval drive bred into them over the centuries. In addition, these breeds predominated in the dog shelters and humane societies used by U.S. Customs as the primary source for its dog procurement, which has not only benefited the Customs' program but the local dog shelters too. Local shelters must by law destroy stray dogs after a certain time period if no one selects or adopts the dog. The Customs' instructors select dogs scheduled to be put to sleep.

The Customs' training method is based on the natural behavior of these retriever breeds of dogs. By using a dog's natural behavior, the instructors can adjust certain aspects of their training program to deal with the individual personality of each dog. Although each dog that entered the training program possessed the same basic qualifications, each

then displayed them in varying degrees of intensity because of personality differences.

During the training process, the other aspect of the program that has ensured success has been maintaining the integrity of the narcotic odor. During the development of the training program there were several incidents when the detector dog would respond to nondrug odors. In those incidents a common factor was identified: The same nondrug odor was also present during the training program. To the dog, the materials that were used in the scent-association process (a process by which the dog identifies the narcotic odor with the tug-of-war game) combined with the drug odor represented a completely different odor picture (a combination of odors that the dog associates with a positive reward). This problem was eliminated by ensuring that all materials used in the training process smelled like the specific drug in question. Additionally, nondrug odor materials are routinely available or added as distractors during many training, certification, and maintenance protocols to ensure that the dogs do not alert to nondrug odors.

In recent years scientific studies have expanded our understanding of the behavioral and chemical basis of canine alerts to specimens and have demonstrated the sensitivity and reliability of detector dog teams. For example, beginning in 1987, reports of cocaine residues on money shed doubts on the validity of using canines to indicate narcotics odor on currency and even the validity of such searches where innocently contaminated currency could illicit a conditioned response by a detector dog team. Detailed scientific studies of the specific chemicals and amounts have subsequently confirmed that most currency in circulation is contaminated with nanogram to microgram quantities of microscopic cocaine residues but that the levels of narcotic odor chemicals emanating from such currency is insufficient to illicit the conditioned response from a narcotic detector dog. These studies have demonstrated that a narcotic detector dog's conditioned response indicates significant recent contamination of the currency by narcotic odor and these responses have been used in courts of law as part of forfeiture proceedings.

Dog selection, the development of a conditioned response, and the integrity of the narcotic odor are all key elements in the employment of dogs as drug detectors. Further information about this type of dog training can be obtained through the U.S. Customs and Border Protection Canine Enforcement Program in Washington, D.C.

See also **Asset Forfeiture; Drug Interdiction; Seizures of Drugs; U.S. Government: Agencies in Drug Law Enforcement and Supply Control; U.S. Government Agencies: U.S. Customs and Border Protection (CBP).**

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DOM. This drug's street name is STP. During the hippie drug culture of the Vietnam War period, its name referred to "serenity, tranquility, and peace." This was also a taunt and a spoof, since the initials were the same as a widely available oil additive that made an automobile engine run smoothly. The drug DOM is a member of a family of hallucinogenic substances based on molecular additions to phenethylamine. This is a group of compounds that have structural similarities to the catecholamine-type neurotransmitters, such as norepinephrine, epinephrine, and dopamine. While our bodies make these catecholamines from dietary amino acids, they do not make the chemical substitutions that produce a psychedelic compound. Mescaline is the best and longest known of this family of hallucinogens.

DOM is a synthesized compound that produces effects similar to mescaline and lysergic acid diethylamide (LSD), but the effects of DOM can last for fourteen to twenty hours, much longer than those of LSD. In addition, the effects of DOM have a very slow onset. Some of the initial street

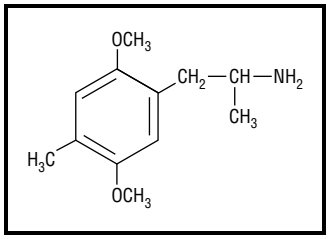

Figure 1. Chemical structure of DOM (STP). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

users of DOM had previous experience with LSD, a drug with a much more rapid onset. When the typical LSD-type effects were not found soon after taking DOM, some users took more drug, which led to a very intense and long-lasting psychedelic experience. Ironically, DOM was originally manufactured in the hope of producing a shorter, less-intense trip than LSD, which, it was thought, might be more useful and manageable in producing a period of insight and self-reflection in psychotherapy. This hope was never achieved.

See also **Designer Drugs; Dimethyltryptamine (DMT).**

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R. N. PECHNICK

DOPAMINE. Dopamine (DA) is a catecholamine according to its chemical structure and a neurotransmitter of special importance for drug addiction. DA is a decarboxylated form of dopa (an amino acid) found especially in the basal ganglia. Chemically known as 3,4 dihydroxyphenylethylamine, DA arises from dihydroxphenylacetic acid (dopa) by the action of the enzyme dopa decarboxylase. DA-containing neurons (nerve cells) are widespread in the brain and the body. DA is also found in minute amounts in other catecholamine neurons as a precursor to norepinephrine. Small DA-containing interneurons are found in the autonomic ganglia, retina, hypothalamus, and medulla. Long axon neurons are found in two extensive circuits: (1) the nigrostriatal pathway, which links the substantia nigra neurons to the basal ganglia neurons and regulates locomotor events; (2) the mesocortical and mesolimbic circuits (i.e., mesocorticolimbic system), which arise in the ventral tegmental area and project to the neocortex, limbic cortices, nucleus accumbens, and amygdala, where they regulate emotional events, including several forms of drug addiction, reinforcement, or reward.

The DA system is important in responding to salient stimuli and facilitating conditioned learning. Stimuli, including non-drug rewards (such as food) and a variety of commonly abused drugs, can activate the mesocorticolimbic system. Acute administration of opioids, nicotine, alcohol, and cannabinoids all facilitate the release of DA in the nucleus accumbens through actions on the ventral tegmental area or the nucleus accumbens directly. Although a wide range of commonly abused drugs stimulate the release of DA, it is important to note that DA is not the sole neurotransmitter involved in reward. The reinforcing effects of the above-mentioned drugs have both DA-dependent and DA-independent mechanisms. This is shown by the fact that the rewarding effects of heroin, nicotine, and alcohol are still present in rodents following inactivation of the mesocorticolimbic DA system.

Psychostimulants, such as amphetamine, methamphetamine, and cocaine, have a direct effect on mesocorticolimbic dopamine by blocking the DA transporter. The DA transporter, which transports DA from outside the nerve terminal to inside the nerve terminal, functions to retrieve released DA and help terminate its actions at receptors. By preventing the reuptake of dopamine, psychostimulants increase the extracellular concentration of DA, thereby facilitating activation of DA receptors. Animal studies have shown that blockade of dopamine receptors with systemically administered receptor antagonists (blockers) reduces the reinforcing effects of psychostimulants. Human subjects, both drug abusers and non-drug abusers, show an increase in striatal extracellular DA when acutely administered a psychostimulant. The increases in DA were associated with increases in self-reported

measures of euphoria by the subjects. Striatal DA is also increased in addicted subjects when exposed to a stimulus associated with the drug (videotaped scenes of subjects taking cocaine). Imaging studies have shown that long-term drug use can result in decreased striatal DA release and alterations in D2 dopamine receptors.

DA is also thought to be involved in schizophrenia and psychosis since DA-receptor-blocking drugs are clinically useful antipsychotic agents. Another disease, in which DA is lost due to the degeneration of DA-containing neurons, is Parkinson's disease, which can be treated by replacing DA with its precursor, dopa.

See also **Neuron.**

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FLOYD BLOOM
REVISED BY MARK MOFFETT (2009)

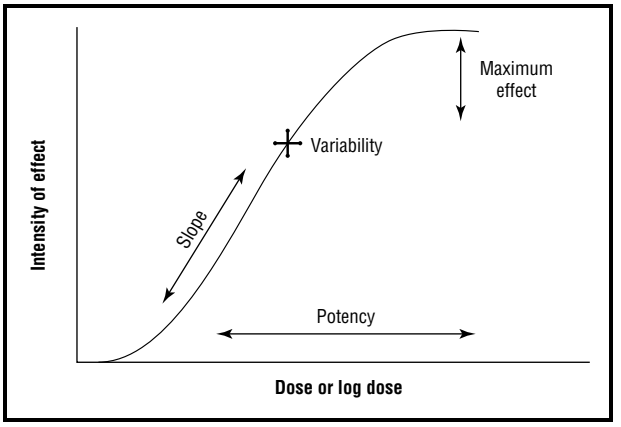

Figure 1. Representative dose-effect curve, with its four characteristics. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

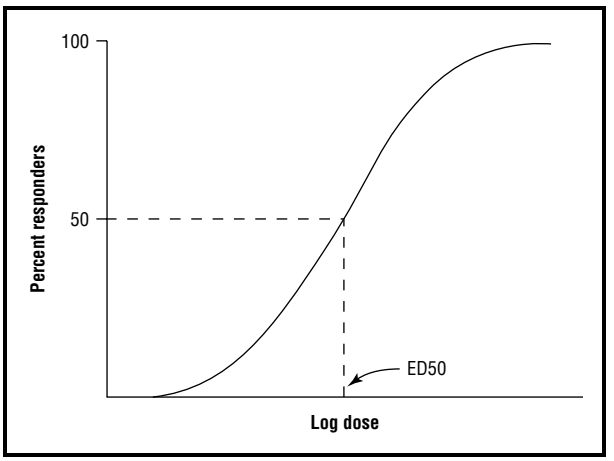

Figure 2. Representative dose-effect curve, showing a median effect dose (ED50). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

DOSE-RESPONSE RELATIONSHIP.

The relationship between the dose (amount) of a drug and the response observed can often be extremely complex, depending on a variety of factors including the absorption, metabolism, and elimination of the drug; the site of action of the drug in the body; and the presence of other drugs or disease. In general, however, at relatively low doses, the response to a drug generally increases in direct proportion to increases in the dose. At higher doses of the drug, the amount of change in response to an increase in the dose gradually decreases until a dose is reached that produces no further increase in the observed response (i.e., a plateau). The relationship between the concentration of the drug and the observed effect can therefore be graphically represented as a hyperbolic curve (see Figure 1).

Often, however, the response (ordinate) is plotted against the logarithm of the drug concentration (abscissa) to transform the dose-response relationship into a sigmoidal curve. This transformation makes it easier to compare different dose-response curves—since the scale of the drug concentration axis is expanded at low concentrations where the effect is rapidly changing, while compressing the scale at higher doses where the effect is changing more slowly (see Figure 2).

Finally, there are two basic types of dose-response relationships. A graded dose-response curve plots the degree of a given response against the concentration of the drug as described above. The second type of dose-response curve is the

quantal dose-effect curve. In this case, a given quantal effect is chosen (e.g., a certain degree of cough suppression), and the concentration of the drug is plotted against the percentage of a specific population in which the drug produces the effect. The median effective dose (ED50 or the dose at which 50% of the individuals exhibit the specified quantal effect) and the median lethal dose (LD50 or the dose at which death is produced in 50% of the experimental animals in preclinical studies) can be estimated from quantal dose-effect curves. With this type of curve, the relative effectiveness of various drugs for producing a desired or undesired effect, as well as the relative safety between various drugs, can be determined. The ratio of the LD50 to the ED50 for a given effect indicates the therapeutic index of a drug for that effect and suggests how selective the drug is in producing its desired effects. In clinical studies, the concentration of the drug required to produce toxic effects can be compared to the concentration required for a specific therapeutic effect in the population to estimate the clinical therapeutic index.

See also **Drug Metabolism; ED50.**

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NICK E. GOEDERS

DOVER'S POWDER.

Dover's Powder, developed and described by the British physician Thomas Dover in 1732, was one of the more popular and enduring of the opium-based medications that were widely used in the United States and Europe prior to the twentieth century. The medication combined opium with what we know today as ipecac (ipecacuanha), a substance that induces vomiting. The result was a pain-reducing potion that might induce a sense of euphoria but could not be ingested in large quantities because of its emetic properties. Taken as a nonprescription medicine by the general public for over 200 years, it was also prescribed by physicians for home and hospital use. Versions of the preparation are still listed in pharmaceutical formularies in which "Dover's Powder" commonly denotes any opium-based mixture that includes ipecacuanha. The wide use of Dover's Powder declined in the early 1900s largely because of the addiction that resulted from the prolonged use of opiates, because of the introduction of other nonaddicting analgesics (painkillers), mainly aspirin, and because of laws regulating sales of opium products.

Thomas Dover (1662–1742) studied medicine at Oxford University in the 1680s. He claimed to have served an apprenticeship with Dr. Thomas Sydenham, the illustrious seventeenth-century practitioner and teacher, who originated the formula for laudanum, another early and popular opium-based medicine. Dover practiced medicine for over fifty years, although during his lifetime he was more famous for his exploits as an adventurer and privateer. His involvement in the early slave trade and in the plundering of Spanish settlements off the coast of South America brought him fortune and fame. On one of his voyages he found the shipwrecked Alexander Selkirk, who, on being returned to London, created a sensation and was to become the inspiration for Daniel Defoe's *Robinson Crusoe*. Dover retired from his merchant sailing career a wealthy man, but poor investments led him to resume his medical career first in Gloucestershire and later in London.

In 1732, probably to attract patients to his new practice in London, Dover published *An Ancient Physician's Legacy to His Country*, one of the earliest medical treatises written for the general public. The book listed forty-two ailments with successful treatments used by Dover, and included the testimonial letters of many "cured" patients. The book enjoyed popular success and was reprinted eight times, the last in 1771, nearly thirty years after his death. One remedy described in the book, the use of mercury, earned him the nickname during his lifetime of the Quicksilver Doctor, but the formula for Dover's Powder, which appears unchanged in all eight editions, has proven to be his most enduring legacy. Appearing on page 18 of the original edition as a treatment for gout, the directions read:

> Take Opium one ounce, Salt-Petre and Tartar vitriolated each four ounces, Ipecacuana one ounce, Liquorish one ounce. Put the Salt Petre and Tartar into a red hot mortar, stirring them with a spoon until they have done flaming. Then powder them very fine; after that slice your opium, grind them into powder, and then mix the other powders with these. Dose from forty to sixty or seventy grains in a glass of white wine Posset going to bed, covering up warm and drinking a quart or three pints of the Posset—Drink while sweating.

Dover's familiarity with opium most probably resulted from his association with Thomas Sydenham and thereby his acquaintance with the benefits of laudanum (an alcoholic tincture of opium). Dover's ingenious use of opium with ipecacuanha seems to have been original. His unique formula, Pulvis Ipecacuanha Compositus, with its specificity of ingredients, produced a relatively reliable and consistent potion in an era when there was no regulation of medications and little standardization in their preparation. Medications could be purchased at apothecary shops with or without doctors' prescriptions or at back-street stores that sold drugs along with food, clothing, and other necessities of life. The major issue at the time in the use of opiate-based medications was not that they contained what we now know to be a narcotic, but whether the consistency of the formula or the misuse by the patient caused overdoses of what could be poisonous ingredients. Dover's Powder provided a stable product that, because of the ipecacuanha, could not be taken in excess at any one time. The powder came to be trusted by the general public and widely prescribed by physicians. It was considered such a safe remedy that it was even prescribed for children.

Although Dover originated his powder as treatment for gout, it was used throughout the eighteenth and nineteenth centuries along with many other opium-based patent and official preparations by large numbers of people for a wide variety of disorders. Opium, used as a healing plant for over 6,000 years, was an ingredient in countless formulas that were openly available and credited with curing the most common disorders of the time. Mixed in a tincture, it was found in laudanum; in a camphorated formula it became paregoric; and it was also included in preparations for lozenges, plasters, enemas, liniments, and other general medications.

Opium-based medicines were used for many disorders, including insomnia, diarrhea, bronchitis, tuberculosis, chronic headache, insanity, menstrual disorders, pain, malaria, syphilis, and smallpox. Often both physicians and patients mistook its narcotic properties, which relieved pain and created a sense of well-being, as curative rather than palliative, and little was understood of the darker side of opiate medications—the destructive nature of addiction—until well into the nineteenth century. By this time, it was common for middle- and upper-class people, especially women and those with chronic diseases, to be addicted to opiates that were frequently seen in innocuous health elixirs or in remedies that had been originally prescribed by physicians. Widespread prescribing by physicians and easy availability of the opiate medications made addiction a frequent result of medical therapeutics.

By the middle of the nineteenth century, the issue of opium addiction began to appear with more frequency in the medical literature, and in both the United States and England there were pressures to regulate both the pharmacy trade and the use of narcotic medications, especially the patent medicines containing opiates. Even then, it was not until the end of the century—as a result of better education of physicians and pharmacists, advances in diagnosis and therapeutics, and a growing understanding of the nature of addiction—that opium-based medications were supplanted by other curative treatments and by nonaddictive salicylate analgesics such as aspirin. Opium-based medicines used today, such as morphine and codeine, are government-regulated and can be purchased legally only by prescription.

Dover's Powder in its original form is now an obsolete medication. It should be recognized for its place in the history of pharmacology as a relatively reputable medicine used from 1732 until the 1930s, an era in which opium-based medications were one of the few remedies that brought relief to suffering patients. Many of these medications came to be misused by both patients and physicians who had little understanding of addiction and few options for pain relief. Thomas Dover, seen as an adventurer and opportunist by many during his lifetime, developed a preparation that allowed patients to use a narcotic while limiting its ingestion. More precise knowledge of the healing as well

as the addictive properties of narcotics allows modern physicians and pharmacologists to deal specifically with the dosage of narcotic medications. Nevertheless, Dover's Powder, an ingenious and effective solution to a thorny problem, became a household name long after its originator's medical career had ended and his medical treatise had been published.

See also **Addiction: Concepts and Definitions; Britain; Opiates/Opioids.**

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DRAMSHOP LIABILITY LAWS.

Dramshops are taverns, saloons, bars, and drinking establishments. All states impose fines and other punishments when alcohol is sold to visibly intoxicated customers or habitual drunkards. Although historically these laws aimed to preserve public order and morality, as of 2008 they were perceived primarily as tools to curtail drunk driving. Their effectiveness is a direct function of compliance and enforcement. Although compliance has rarely been studied, one study in Michigan found that an increase in police enforcement (through visits and warnings) resulted in a three-fold increase in the rates of service refusal to intoxicated patrons. In addition, service intervention training has been voluntarily implemented in many states and is required by law in some. Although the evidence is mixed, some research indicates that sustained server training can reduce the risk of drunk driving.

In addition to these statutory penalties, more than half the states also impose tort liability on tavern keepers for injuries caused to third parties by intoxicated patrons. Liability in such situations serves both compensatory and deterrent purposes. In the first comprehensive analysis of dramshop liability laws, Frank Sloan (2002) concludes that they are more effective than either administrative or criminal regulation in changing the behavior of those who serve alcohol. As a consequence, these laws reduce alcohol-related traffic fatalities. Vendors of alcohol must also balance the costs of liability insurance under a dramshop act by increasing drink prices. More than thirty states and many cities have extended the dramshop principle to private so-called social hosts who fail to take adequate precautions to prevent obviously intoxicated guests from getting behind the wheel.

The threat of liability for servers of alcohol appears to exert a deterrent effect. These laws also serve an important pedagogical effect. Together with other legal and cultural factors, dramshop laws help to shape social norms against driving while intoxicated.

See also **Alcohol: History of Drinking (International); Alcohol: History of Drinking in the United States; Driving, Alcohol, and Drugs; Driving Under the Influence (DUI); Drug Interactions and Alcohol; Drug Testing Methods and Clinical Interpretations of Test Results; Legal Regulation of Drugs and Alcohol; Mothers Against Drunk Driving (MADD); Students Against Destructive Decisions (SADD).**

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FREDERICK K. GRITTNER (2009)

DREAMS/DREAMING.

See **Sleep, Dreaming, and Drugs.**

DRIVING, ALCOHOL, AND DRUGS.

Injuries, especially from motor vehicle collisions, are the leading cause of death for individuals under age 44. The presence of alcohol is the factor most frequently associated with fatalities in vehicle crashes, drownings, falls, and fire, according to the U.S. Department of Health and Human Services (1987). In the first report of the U.S. Department of Transportation to Congress on traffic safety and alcohol (in 1968), it was concluded that more than 50 percent of fatal traffic collisions and 33 percent of serious-injury traffic collisions were alcohol-related.

EARLY STUDIES AND SUCCESSES

Although the association between alcohol consumption and traffic accidents had been recognized by the beginning of the twentieth century, the magnitude of the problem did not capture public attention until the 1970s, when public tolerance of driving under the influence of alcohol (DUI) decreased sharply. This shift in attitude, combined with increased legal countermeasures, resulted in a significant decline in alcohol-related traffic fatalities (among drivers, passengers, pedestrians, etc.) from a high of 60 percent in 1982 to 40 percent by 1997 of traffic fatalities with victims who had alcohol present. Similarly, the proportion of alcohol-involved drivers in traffic fatalities declined from 41 percent in 1982 to 24 percent in 1997, according to the Department of Transportation's *Traffic Safety Facts 2005.*

Unfortunately, there has been a halt in this decline since 1997, and little progress in reducing alcohol-related accidents and fatalities occurred between the mid-1990s and the late 2000s. This has been reflected not only in the U.S. data but throughout the majority of industrialized nations. Thus, alcohol still remains the single largest factor in traffic fatalities and serious injuries.

BLOOD ALCOHOL CONCENTRATION AND DRIVING

Voas and colleagues (1998) compared the relative frequency of driving under the influence of alcohol in three U.S. nationwide surveys, done in 1973, 1986, and 1996 on weekend nights. Drivers were stopped at random and asked to provide breath samples for alcohol testing. The blood alcohol concentrations (BACs) from the three surveys were compared regarding time, day, gender, age, ethnicity, geographical region, and other factors. Across nearly all population subgroups, the presence of alcohol in nighttime weekend drivers dropped from 36 percent in 1973 to 26 percent in 1986, and then to 17 percent in 1996. However, although the percent of decline for drivers with BACs below 0.10 percent was 54 percent from 1973 to 1996, there was only a 45 percent decline in drivers with over 0.10 percent BAC.

Epidemiological studies have compared the BACs of collision-involved drivers with those of randomly selected drivers passing the collision site at similar times. These studies have demonstrated that the probability of a crash increases with any departure from zero BAC, and that it increases exponentially with increasing BAC levels. By the time BAC levels exceed 0.20 percent (200 mg/100 mL), the probability of a collision increases more than 100 times, or 10,000 percent.

Most areas of human behavior are eventually impaired by increasing alcohol levels. However, the examination of alcohol-related collision data from governmental investigations and police collision reports suggests that information-processing errors are common in the majority of alcohol-related traffic collisions. Information-processing deficits include impairment of attention, visual search, and perception. The second largest category of errors involves errors in judgment, such as speed selection. Failure to control a car because of decreasing motor skills remains a distant third cause of crashes, despite the popular assumption that links driving impairment with the appearance of intoxication and motor incapacitation.

The results observed in epidemiological survey studies are supported by numerous experimental studies in which driver behavior was examined under controlled conditions. Such studies may examine one or two driving relevant behaviors in laboratories, or they may be more complex studies of driving-related behavior using driving simulators or closed-course driving situations that preserve the safety of the driver.

AREAS OF IMPAIRMENT

Moskowitz and Robinson (1988) reviewed 177 experimental studies of alcohol's effects on driving-related behaviors that met criteria of scientific merit. The behavior found to be most affected by alcohol was divided attention, with impairment seen even at alcohol levels below 0.02 percent (20mg/100mL). Divided-attention tasks involve simultaneously monitoring and responding to more than one source of information, which is characteristic of many complex man-machine interactions, such as driving and flying. While operating a vehicle, drivers under the influence of alcohol frequently fail to detect significant potential threats in the environment.

Similarly, studies have indicated that information processing and perception are affected at low BAC levels. Tracking, which is analogous to car-control functions such as maintaining a heading and lane position, has been shown to be impaired at low BACs when performed simultaneously with other functions in divided-attention situations, though this ability is less impaired when the tracking task is performed by itself. Complex reaction-time tasks involving several competing stimuli and responses are impaired at low BACs, whereas simple reaction-time tasks requiring little information processing are more resistant to the effects of alcohol.

Studies of psychomotor skills in driving simulators and closed-course driving studies have shown considerable variation in the BAC levels at which impairment appears. These variations are likely explained by the differences in information-processing requirements among these varied tasks. The Moskowitz and Robinson review concluded that there is no minimum threshold for alcohol's impairment of complex human-machine tasks. Thus, any reliable measure of alcohol in the human system produces some impairment.

Other areas that have been suggested as leading to alcohol-related accidents include poor judgment and violent and aggressive behavior. Both laboratory studies and epidemiological data, such as the incidents of alcohol in violence, have provided evidence that the effects of alcohol on aggression are significant. On the other hand, because of the difficulties in modeling the behavior, few studies have been performed in the laboratory on the effect of alcohol on judgment. Nonetheless, laboratory studies have indicated significant impairment at low BAC levels, and epidemiological studies have shown increased crash frequency at BAC levels below those at which the majority of the population would exhibit symptoms of intoxication, such as slurred speech and unsteady gait. Thus, the absence of signs of intoxication is not evidence that a driver is capable of operating a motor vehicle or other machinery safely.

In 2000, Moskowitz and Fiorentino updated Moskowitz and Robinson's 1988 report with a review of an additional 112 studies published from 1981 to 1997. Although the main conclusions of the 1988 report were confirmed, this review found more frequent reports of impairments at very low alcohol levels, reflecting improvements in the sensitivity and reliability of scientific investigation. Moreover, new behavioral areas are being explored, such as the tendency to fall asleep at the wheel, which increases significantly even at low BAC levels.

OTHER DRUGS

The major involvement of alcohol in traffic accidents and other injuries is well documented. However, it is a bit more difficult to draw conclusions about the role of drugs other than alcohol in traffic safety. Although laboratory studies on the effects of many drugs are similar to alcohol in demonstrating the impairment of performance skills, there are difficulties in executing epidemiological studies on the effects of drugs in driving. For example, few non-crash-involved drivers volunteer to provide blood samples so that their drug levels can be compared with blood samples obtained from collision victims. This makes it difficult to perform studies comparing blood-drug levels.

While studies have been completed in hospitals comparing blood-drug levels in trauma patients involved in driving collisions with blood-drug

samples from volunteers who were in the hospital for other reasons, serious questions arise regarding the representativeness of the control group. Another problem in relating drug use to vehicle crashes has been the difficulty of evaluating the behavioral significance of blood-drug levels. Unlike alcohol, where levels in venous blood samples or breath samples are essentially equivalent to those from blood in the brain (the site of drug action), for most other drugs there is a complex relationship between blood level and the magnitude of behavioral impairment. Many drugs remain present in the blood for weeks beyond any period in which behavioral effects may be observed. In other cases, drug levels in the blood drop extremely rapidly and become difficult to detect, while behavioral impairment remains. Thus, many epidemiological studies of drugs and driving report the presence of the drug rather than the level of drug concentration.

One technique to circumvent control-group problems has been to assign responsibility or nonresponsibility to crash-involved drivers, and to then correlate the presence of drugs with the frequency of crash responsibility. Within the constraints of these epidemiological studies, researchers have often concluded that tranquilizers, antihistamines, and antidepressants are overrepresented in crash-involved drivers. Terhune and colleagues (1992) examined the presence of drugs in blood specimens from 1,882 fatally injured drivers. Both illicit and prescription drugs were found in 18 percent of the fatalities, while marijuana was found in 6.7 percent, cocaine in 5.3 percent, tranquilizers in 2.9 percent, and amphetamines in 1.9 percent.

When crash responsibility was assigned and correlated with drug use, the small number of individuals in each separate drug classification made statistical significance difficult to obtain, despite the fact that several drug categories were associated with increased crash responsibility. Crash-responsibility rates did increase significantly as the number of drugs in the driver increased. Many of the drug users in the Terhune study used several drugs simultaneously, and these drivers had the highest collision rates. Alcohol, meanwhile, was found in 52 percent of the fatalities, with more than 90 percent of the drivers with BACs over 0.08 percent considered responsible for the crash.

MARIJUANA

Since the 1950s, the most frequently used illicit drug in the United States has been marijuana. Epidemiological studies have demonstrated that it is also the drug most frequently consumed by drivers. Bates and Blakely (1999) reviewed the epidemiological literature for marijuana's role in motor vehicle crashes. They concluded that there is no evidence marijuana alone increased either fatal or serious-injury crashes. However, the evidence is inconclusive whether the presence of marijuana in combination with alcohol increases fatalities or serious injuries over the number produced by alcohol alone. Nor was it possible to determine whether marijuana increases the rate of less serious vehicle crashes.

Baldock's 2007 review of the literature on marijuana and crash risk reached similar conclusions. The many methodological problems involved in obtaining blood samples from crash-involved drivers and from a comparable representative sample of control drivers led the author to conclude that no existing study was conclusive, and that the driving risk associated with marijuana "remains to be determined."

SKILLS PERFORMANCE

In contrast to the ambiguity of scientific information available from epidemiological sources about the role of drugs in causing collisions, numerous experimental studies have been performed to evaluate the effects of drugs on skills performance. Regulatory agencies in many countries have frequently required an evaluation of the side effects of prescription drugs on the performance of various skills, and several governments have supported studies of the effects of illicit and abused drugs on skills performance in the laboratory.

Thus, the evaluation of the effects of drugs on driving and other human-machine interactions has depended primarily on experimental studies in which changes in behavior can be observed as a function of differences in administered doses and the time after administration. However, no other drug has been evaluated in as extensive a range of behaviors as has alcohol. Nevertheless, many drugs have been studied with respect to some important variables required for driving.

The emphasis in these drug studies has tended to be on the evaluation of vision, attention,

vigilance, and psychomotor skills. Driving-simulator studies have also been done on occasion. The psychomotor skill most often examined has been some form of tracking. Reviewing this literature presents considerable difficulties, however, because there are so many differences between classes of drugs, as well as between individual drugs within the same drug classification. For example, many minor tranquilizers, especially benzodiazepines, have been shown to impair attention and tracking in a wide variety of studies. However, newer tranquilizers, such as buspirone, exhibit little evidence of impairment.

Conclusions about impairments in a drug category are likely to change due to the pressures exerted by the drug regulatory agencies on drug companies to develop medicines that do not impair skills performance. Most hypnotics exhibit residual skills impairment the day following use, but new drugs have been introduced whose duration of effects is shorter, so there will be less residual impairment after awakening.

Another class of psychoactive drugs, the antidepressants, especially amitriptyline, has long been known to impair performance in a variety of skills. Again, recently introduced types of antidepressants do not produce the same degree of impairment. Although narcotic analgesics derived from opium (opiates) have been shown experimentally to lead to decreased alertness, chronic use produces considerable tolerance to some side effects, which may explain why epidemiological studies have not found consistent evidence of differences in crash rates between narcotic users and control groups. Moreover, patients maintained on a stabilized dosage of methadone, a synthesized narcotic, have shown little evidence of impairment in a wide variety of experimental and epidemiological studies.

Another category of drug that shows evidence of impairing skills performance in laboratory studies is the antihistamines, many of which produce impairment of performance accompanied by complaints of drowsiness and lack of alertness. Again, recent pharmacological advancements have produced antihistamine drugs which maintain antihistamine actions but have difficulty crossing the blood-brain barrier and thus produce little impairment. One such drug is loratadine (Claritin).

Of all the illicit drugs, marijuana has had the largest number of experimental studies performed to examine its effects. Many of these studies indicate that marijuana impairs coordination, tracking, perception, and vigilance. It has also been shown to impair performance in driving simulators and on-the-road studies. Yet, epidemiological studies have been inconclusive in demonstrating increased crash risk, perhaps due to the relatively brief duration of elevated blood THC levels or perhaps due to compensatory behaviors as observed in several simulator studies.

Although there has been concern over an increased use of stimulants such as amphetamines and cocaine among drivers, there is little experimental evidence demonstrating driving impairment with these drugs. On the contrary, most studies of these stimulants, as well as of caffeine, indicate an improvement in skills performance. However, with the chronic (long-term) use of stimulants, an increased dose must be taken as tolerance develops. Thus, the dose levels examined in the laboratory may not reflect those found among drivers. In addition, after the stimulation phase, a subsequent depressed phase occurs (called the "crash"), with increased drowsiness and lack of alertness. The stimulant drugs have not been well studied in relation to driving and this needs to be remedied. Further study is needed, both for acute (one-time) use and chronic use.

See also **Alcohol: Chemistry and Pharmacology; Benzodiazepines; Blood Alcohol Concentration; Cocaine; Dose-Response Relationship; Dramshop Liability Laws; Driving Under the Influence (DUI); Marijuana (Cannabis); Minimum Drinking Age Laws; Mothers Against Drunk Driving (MADD); Opiates/Opioids; Psychomotor Effects of Alcohol and Drugs; Social Costs of Alcohol and Drug Abuse; Students Against Destructive Decisions (SADD).**

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DRIVING UNDER THE INFLUENCE (DUI).

Driving under the influence is defined in the statutes of fourteen states as incapacity, meaning that the influence of a drug leaves a driver incapable of driving safely. Specific blood-alcohol concentration (BAC) limits are associated with a DUI offense. As of 2008, all fifty states, the District of Columbia, and Puerto Rico have reduced the legal BAC limit from .10 percent to .08 percent.

The FBI reports that 1,460,498 people were arrested for DUI in 2006. The National Survey of Drug Use and Health, a household survey of approximately 30.5 million people aged twelve and older, indicates that an estimated one in ten (12.4%) reported driving under the influence at least once in the past year. Males were twice as likely as females to report drinking and driving and nearly half were aged eighteen to twenty-five.

An individual with a BAC of .08 percent or higher is eleven times more likely than an individual who has had nothing to drink to be involved in a fatal crash. An analysis of crash fatality data from the National Highway Traffic Safety Administration (NHTSA) shows that the number of persons killed in alcohol-related crashes jumps sharply when the highest BAC involved reaches .08 percent or higher.

The total number of fatalities in alcohol-related crashes decreased 33 percent from 26,173 in 1982 to 17,602 in 2006. NHTSA reports that nearly half (41%) of the total traffic fatalities that year were alcohol-related and an estimated three-fourths involved a driver with a BAC of .08 percent or greater. Drivers involved in fatal crashes with a BAC of .08 or higher in 2006 were most likely to be male and aged twenty-one to forty-four. One in four young drivers (fifteen to twenty years old) who died in motor vehicle crashes that year had a BAC of .08 or higher. NHTSA also projected that three out of ten Americans would be involved in an alcohol-related crash sometime in their lives.

See also **Breathalyzer; Dramshop Liability Laws; Driving, Alcohol, and Drugs; Drug Interactions and Alcohol; Mothers Against Drunk Driving (MADD); Remove Intoxicated Drivers (RID-USA, Inc.); Students Against Destructive Decisions (SADD).**

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DROPOUTS AND SUBSTANCE USE.

Governments and the international community view education as essential in reducing social inequities and poverty worldwide and promoting a more peaceful and sustainable future for all. Yet there is not a country in the world that does not experience the problem of young people dropping out of high school. Research, mostly conducted in the developed world, has attempted to investigate why so many young people drop out of high school by examining the relationship between this behavior and a number of factors that have been found to be associated with leaving school early. One of these factors is substance use.

A REVIEW OF THE LITERATURE

A 2007 review of 46 international research studies conducted by Loraine Townsend and others examined the link between substance use and dropping out of high school. The cross-sectional studies that were reviewed found that high school dropouts were more likely than high school graduates to report tobacco use (cigarette smoking), to report cigarette smoking at an early age, and to be heavy smokers. Furthermore, dropouts and students at risk for dropping out reported higher levels of alcohol consumption and more current and lifetime marijuana use than did in-school students and high school graduates. Compared to high school graduates, and in some cases to General Equivalency Diploma holders, dropouts were more likely to have injected a drug recently, and to have a history of injecting drug use.

Tobacco Use. The longitudinal studies in the review that followed high school dropouts and graduates into early adulthood provide evidence of the unique effect of tobacco use (cigarette smoking) on high school dropout rates, after taking into account a number of other factors that could possibly explain this effect. These factors were: age, gender, family structure, problem behavior, peer influence, and school-related factors such as poor school performance, poor commitment to school, and motivation to perform well at school. While some longitudinal studies in the review found that alcohol use was a factor in dropping out, other studies found that such factors as family and academic background, parental care, truancy, deviant behavior, and school environment had more to do with why some students drop out of school than alcohol use alone.

Studies conducted in Australia and the United States found a strong association between the frequency of early marijuana use and dropping out of school. Even when taking into account other possible explanations, such as other drug use and alcohol consumption, the use of marijuana remained a unique predictor of high school dropout. Furthermore, one study conducted by Helen E. Garnier, Judith A. Stein, and Jennifer K. Jacobs found that teenage drug use was among a number of predictors. However, other studies were able to demonstrate that dropping out of high school had more to do with adopting age-inappropriate roles—such as early marriage, pregnancy, and parenthood—than with drug use alone.

The Townsend review also found evidence that some high school dropouts continued to use tobacco as they got older, whereas the rates of tobacco use among high school graduates declined over time. Researchers in the United States found that dropping out of high school was strongly related to an increased risk of adult-onset alcohol abuse and dependence. This association persisted even when the early onset of alcohol problems was taken into account. Findings from one study conducted in Australia suggest that dropping out of high school does not lead to an increase in marijuana use soon after dropping out. On the other hand, findings from three studies conducted in the United States found that dropping out of high school leads to an increase in marijuana use in the long term (Ensminger et al., 1996; Green & Ensminger, 2006; Kogan et al., 2005).

Substance Abuse. The findings from the studies that were part of the review suggest that there is a

strong link between substance use and dropping out of high school. Not only is it possible that substance use leads to dropping out of school, but also that dropping out of school leads to substance use or an increase in substance use. However, the problem with this overall conclusion is that it gives the impression that all dropouts resist conforming to the demands of educational systems and engage in (or begin to engage in) deviant behaviors. This picture is highly inaccurate, as it does not take into account the fact that a great many of the young people who drop out of high school do not use substances and do not engage in deviant behavior. The studies reviewed by Townsend and colleagues revealed that many more dropouts were not using substances than were. Evidently, there are protective factors that provide some high school dropouts with the ability to resist maladaptive behaviors, and indeed to succeed in their daily lives. Little research on these protective factors has been conducted to date, however.

THEORIES OF SUBSTANCE USE AMONG DROPOUTS

In addition to the evidence from research studies, a number of theories have been put forward to try to explain the role that substance use may play in the dropout phenomenon. Some of the more commonly cited theories are listed here.

Social control theory. This theory proposes that when the moral bonds that tie people together, and that tie people to accepted social norms, are broken, mechanisms that were customarily used to restrain antisocial behavior no longer operate. When this happens, people are more likely to deviate from societal norms by, for example, using illicit drugs or consuming excessive amounts of alcohol. They are also more likely to have a poor commitment to conventional social groups (such as families) and institutions (such as schools). From this perspective, the relationship between substance use and dropping out of high school would be explained by a weakening of the social controls that operate within families and schools to discourage antisocial behavior such as substance use and dropping out of school.

Problem-prone behavior and general deviancy theory. This theory describes dropping out of high school and substance use as just two of a number of nonconformist, deviant behaviors to which certain adolescents are prone. From this perspective, adolescents who hold nonconformist attitudes and values are also more likely to engage in a variety of other nonconformist behaviors, such as smoking, drug and alcohol use, and abandoning the student role. A number of studies in the Townsend review were able to demonstrate that substance-using adolescents are at risk for a variety of other problem behaviors, such as dropping out of school, truancy, perpetrating and being victims of violent behavior, early sexual involvement, and mental health problems.

Primary socialization theory. This theory proposes that adolescents are most at risk when ties to school and family are weak and ties to peers are strong, particularly when their peers use substances or are dropouts.

Social learning theory. This theory is similar to the primary socialization theory. The theory proposes that when social bonds are weak, learning processes occur within peer groups such that delinquent socialization becomes the strongest learning influence. This leads to deviant behaviors, including substance use and dropping out of high school.

Peer cluster theory. This theory proposes that problems at school are a dominant factor in creating deviant peer groups or clusters. Those students experiencing academic or disciplinary problems at school have a way of seeking each other out and forming peer groups. These peer groups encourage, support, and normalize a range of deviant behaviors and attitudes, such as substance use and dropping out of school, by means of social learning processes.

The theory of differential association. This theory is similar to peer cluster theory, except that it proposes substance use, rather than problems at school, as the mechanism that brings substance-using peers together. The newly found peers act as role models and reinforce behaviors that increase the likelihood of dropping out of school.

Deviant affiliation theory. This theory proposes that adolescents who have strong affiliations

to delinquent and substance-using peers are encouraged to exhibit the same behaviors.

Strain theory. This theory explains how adolescents who are experiencing problems at school such as poor or failing grades, seek out alternative self-defining behaviors that are often deviant in nature, such as substance use. From this perspective, school failure, poor academic performance, dissatisfaction with school, and high rates of substance use should all be strongly related to dropping out.

While all these theories provide some explanation of the relationship between substance use and high school dropout, there is no one theory that provides us with a clear explanation of the link between dropping out and substance use alone. There are a number of possible reasons for this. First, the dropout phenomenon is highly complex and has many possible explanations, only one of which may have to do with substance use. Second, theories and research to date may not have accounted for all the possible explanations for the dropout–substance use relationship. For example, obvious biological explanations may account for the relationship between dropping out and alcohol use, marijuana use, and other illicit drug use (Lynskey & Hall, 2000). These explanations would include the effects of alcohol, marijuana, and illicit drug use on such phenomena as motivation and cognitive functioning. However, the same cannot be said for the relationship between tobacco use and high school dropout. It is likely that some as yet undetected factors may be associated with an increased risk of tobacco use and dropping out of school.

Third, the people who dropped out of the longitudinal studies over time, and for whom there was therefore no information, were often overrepresented by socially disadvantaged people, poor people, school dropouts, and drug users. These are the people most at risk for dropping out and substance use, and excluding their information from research findings may have resulted in incomplete or inaccurate explanations of the relationship between dropping out of high school and substance use. Finally, researchers in Australia have suggested that future studies should explore the experiences and opinions of those who drop out of school in searching out ways to address the problem (Shacklock, Smyth, & Wilson, 1998; Smyth, 2005; Smyth & Hattam, 2001). These researchers suggest that research to date may have been focusing too much on factors that are not relevant to the dropouts themselves.

In spite of these limitations, the theories and research findings do suggest areas of focus for high school dropout and substance use prevention efforts. Many of the theories suggest weakened bonds to conventional society and institutions as reasons why students drop out of school or use illicit substances. Strengthening ties to and creating a commitment to conventional institutions such as school may go a long way to reducing the dropout and substance use problems. To this end, academic achievement programs may not only reduce school dropout rates, they may also reduce the rates and levels of teenage substance use. Several research groups have investigated whether intervention programs directed at first- and second-graders might change their risk for later drug use, conduct problems, and dropping out. Other research groups have targeted high-risk elementary and middle school students, giving them and their families special programs to promote learning and a sense of mastery over schoolwork.

Given that dropout rates are not declining, and are in fact increasing in some parts of the world, some researchers have suggested that student-focused programs have limited effectiveness. They suggest that research should shift its focus from students' life circumstances—such as their families, their attitudes towards school, and their motivations to perform well at school—and begin to examine schools themselves. What schools offer young people, the way in which it is done, and what students and dropouts themselves have to say about school are areas of possible research.

The range of unfortunate effects of dropping out of school makes it important to sustain stay-in-school programs as well as outreach programs for youth who are chronically absent from school or who have dropped out before graduation. At the same time, it is important for governments and the international community to investigate schools, and school systems themselves, as possibly contributing to the dropout phenomenon.

See also **Alcohol; Amotivational Syndrome; Marijuana (Cannabis); Tobacco.**

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DRUG. As a therapeutic agent, a drug is any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of disease. It is also a general term for any substance, stimulating or depressing, that can be habituating. According to the U.S. Food, Drug, and Cosmetic Act, a drug is (1) a substance recognized in an official pharmacopoeia or formulary; (2) a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; (3) a substance other than food intended to affect the structure or function of the body; (4) a substance intended for use as a component of a medicine but not a device or a component, part, or accessory of a device.

Pharmacologists consider a drug to be any molecule that, when introduced into the body, affects living processes through interactions at the molecular level. Hormones can be considered to be drugs, whether they are administered from outside the body or their release is stimulated endogenously. Although drug molecules vary in size, the molecular weight of most drugs falls within the range of 100–1,000, since to be a drug it must be absorbed and distributed to a target organ. Efficient absorption and distribution may be more difficult when drugs have a molecular weight greater than 1,000. The drug's molecular shape is also important, since most drugs interact with specific receptors to produce their biological effects. The shape of the receptor determines which drug molecules are capable of binding. The shape of the drug molecule must be complementary to that of the receptor to produce an optimal fit and, therefore, a physiological response.

Within this general definition, most poisons would be considered to be drugs. Although water and oxygen technically fit this general definition and are used therapeutically and discussed in pharmacology textbooks, they are rarely considered to be drugs. Efforts have been made to develop a

more restricted definition, but because so many molecules and substances can affect living tissue, it is difficult to draw a sharp line.

See also **Inhalants; Plants, Drugs From; Vitamins.**

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DRUG ABUSE REPORTING PROGRAM (DARP). The Drug Abuse Reporting Program (DARP) began in 1969 as a comprehensive study that included intake and during-treatment information on individuals entering a drug treatment system established under the U.S. Narcotic Addict Rehabilitation Act of 1966. The DARP was the first national effectiveness evaluation of these new community-based treatments, conducted prospectively at Texas Christian University over a period of twenty years. The study strategy included four distinct phases of research: (1) describing major treatment modalities and the characteristics of drug abusers entering them in the early 1970s, (2) describing during-treatment performance measures and how they related to differences in treatments and clients, (3) describing post-treatment outcomes and how they related to differences in treatments and clients, and (4) describing important elements of long-term addiction careers.

The DARP data system contained records on almost 44,000 admissions during 1969 to 1973 at fifty-two federally supported treatment agencies located across the United States. The study population consisted of clients from major treatment modalities—methadone maintenance programs, therapeutic community, outpatient drug-free, and detoxification—as well as a comparison intake-only group.

THE EFFECTIVENESS OF DRUG-ABUSE TREATMENT

Initial research in this twenty-year project focused on ways of measuring characteristics of treatments, clients, and behavioral outcomes (see Sells, 1975). It was found that drug use and criminal activities decreased significantly during treatment, including outpatient as well as residential programs. More important, the effects continued after treatment ended. Some 6,402 clients located across the United States were selected for follow-up an average of three years after leaving DARP treatment (and 83 percent were relocated). Methadone maintenance, therapeutic communities, and outpatient drug-free programs were associated with more favorable outcomes among opioid addicts than outpatient detoxification and intake-only comparison groups; however, only clients who remained in treatment three months or longer showed significant improvements after treatment. Numerous studies of these data helped establish that treatment is effective and that the longer clients stay in treatment, the better they function afterwards (see Simpson & Sells, 1982).

LONG-TERM OPIOID ADDICTION CAREERS

To study long-term treatment outcomes, a sample of 697 daily opioid (primarily heroin) users were followed up with again, at twelve years after entering treatment (and 80 percent were relocated). It was found that about 25 percent of the sample was still addicted to daily opioid use in year twelve. Length of addiction (defined as the time between first and last daily opioid use) ranged from one to thirty-four years. Of the total sample, 50 percent was addicted nine-and-a-half years or longer, yet 59 percent never had a period of continuous daily use that exceeded two years. Only 27 percent reported continuous addiction periods that lasted more than three years.

Three-fourths of the addicts studied had experienced at least one relapse to daily opioid use. Among those who had ever temporarily quit daily opioid use, 85 percent had done so while in a drug-abuse treatment, 78 percent had quit while in a jail or prison, 69 percent had temporarily quit on their own (without treatment), and 41 percent had quit while in a hospital for medical treatment. The most frequent reasons cited for quitting addiction the last time involved psychological and emotional problems. Ex-addicts reported they had become

tired of the hustle (rated as being important by 83 percent of the sample) and needed a change after hitting bottom (considered important by 80 percent). Other reasons cited as being important were personal or special events such as a marriage or the death of a friend (64 percent), fear of being sent to jail (56 percent), and the need to meet family responsibilities (54 percent) (see Simpson & Sells, 1990, for further details).

The DARP findings have been widely used to support continued public funding of drug-abuse treatments and to influence federal drug policy in the United States. Other similar national treatment evaluation studies were planned and undertaken in the 1980s (Treatment Outcome Prospective Study; TOPS) and in the 1990s (Drug Abuse Treatment Outcome Studies; DATOS) in the United States, as well as in the 1990s in England (National Treatment Outcome Research Study; NTORS). Subsequent research has advanced to increasing understanding of the particular elements of treatment that are most effective and how they can be improved.

See also **Drug Abuse Treatment Outcome Studies (DATOS); Narcotic Addict Rehabilitation Act (NARA); Treatment Outcome Prospective Study (TOPS).**

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D. DWAYNE SIMPSON

DRUG ABUSE SCREENING TEST (DAST). The assessment of drug use and related problems is important for both prevention and clinical care. Measures that are both reliable and valid provide tools for health education, for identifying problems (early if possible) in health care and community settings, and for evaluating the effectiveness of treatment. As well, this information is useful for matching individual needs and readiness for change with tailored interventions.

The Drug Abuse Screening Test (DAST) was designed to be used in a variety of settings to provide a quick index of drug-related problems. The DAST yields a *quantitative* index of the degree of consequences related to drug abuse. This instrument takes approximately 5 minutes to administer and may be given in questionnaire, interview, or computerized formats. The DAST provides a brief, self-report instrument for population screening, identifying drug problems in clinical settings and treatment evaluation.

DAST-20 and DAST-10 Versions. The DAST was modeled after the widely used Michigan Alcoholism Screening Test. Measurement properties of the DAST were initially evaluated using a clinical sample of 256 drug-alcohol-abuse clients (Skinner, 1982). The 20-item DAST has excellent internal consistency reliability (alpha) at 0.95 for total sample and 0.86 for the drug-abuse sample. Good discrimination is evident among clients classified by their reason for seeking treatment. Most clients with alcohol-related problems scored 5 or below, whereas the majority of clients with drug problems scored 6 or above on the 20-item DAST. The DAST-10 correlates very highly (r=0.98) with the longer DAST-20 and has high internal consistency reliability for a brief scale (0.92 for the total sample and 0.74 for the drug-abuse sample).

Subsequent research has evaluated the DAST with various populations and settings including psychiatric patients (Cocco & Carey, 1998; Maisto et al., 2000; Staley & El Guebaly, 1990), prison inmates (Peters et al., 2000), substance-abuse patients (Gavin et al., 1989), primary care (Maly, 1993), in the workplace (El-Bassel et al., 1997), and adapted for use with adolescents (Martino et al., 2004). Overall, these studies support the reliability and diagnostic validity of the DAST in diverse contexts.

Advantages

1. The DAST is brief and inexpensive to administer. Versions are being developed in different languages (French and Spanish).
2. It provides a quantitative index of the extent of problems related to drug abuse. Thus, one may

move beyond the identification of a drug problem and obtain a reliable estimate of the degree of problem severity.

3. The DAST has been evaluated and demonstrated excellent reliability and diagnostic validity in a variety of populations and settings.
4. Routine administration of the DAST would provide a convenient way of recording the extent of problems associated with drug abuse, ensuring that relevant questions are asked of all clients/patients.
5. The DAST can provide a reference standard for monitoring changes in the population over time, as well as for comparing individuals in different settings.

Limitations

1. Since the content of the DAST items is obvious, individuals may fake results.
2. Since any given assessment approach provides an incomplete picture, there is a danger that DAST scores may be given too much emphasis. Because the DAST yields a numerical score, this score may be misinterpreted.

Administration, Scoring and Interpretation. The DAST may be administered in a questionnaire, interview, or computerized format. The questionnaire version allows the efficient assessment of large groups. The DAST should not be administered to individuals who are presently under the influence of drugs, or who are undergoing drug withdrawal. Under these conditions the reliability and validity of the DAST would be suspect. Respondents are instructed that "drug abuse" refers to (1) the use of prescribed or over-the-counter drugs in excess of the directions and (2) any nonmedical use of drugs. The various classes of drugs may include cannabis, (e.g., marijuana, hash), solvents or glue, tranquillizers (e.g., valium), barbiturates, cocaine, stimulants, hallucinogens (e.g., LSD), or narcotics (e.g., heroin). Remember that the questions do not refer to the use of alcoholic beverages.

The DAST total score is computed by summing all items that are endorsed in the direction of increased drug problems. Guidelines for interpreting DAST scores and recommended action are given in Table 1. A score of 3 or more on the DAST-10 and 6 or more on the Dast-20 indicates the likelihood of substance abuse or dependence (e.g., *DSM-IV*, American Psychiatric Association). This diagnosis would need to be established by conducting a further diagnostic assessment.

	DAST-10	DAST-20	Action	ASAM*
None	0	0	Monitor	
Low	1–2	1–5	Brief counseling	Level I
Intermediate (likely meets DSM** criteria)	3–5	6–10	Outpatient (intensive)	Level I or II
Substantial	6–8	11–15	Intensive	Level II or III
Severe	9–10	16–20	Intensive	Level III or IV

*ASAM–American Society of Addiction Medicine Placement Criteria
**DSM-IV–American Psychiatric Association

Table 1. DAST Interpretation Guide. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Availability. Copies of the DAST may be obtained from the Centre for Addiction and Mental Health in Toronto, Ontario (http://www.camh.net).

See also **Treatment, Stages/Phases of: Screening and Brief Intervention.**

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HARVEY A. SKINNER

DRUG ABUSE TREATMENT OUTCOME STUDIES (DATOS).

This family of studies is designed to provide comprehensive information on continuing and new questions about the effectiveness of the drug-abuse treatment that is available in a variety of publicly funded and private programs. These data update and augment the information available from earlier national studies, such as the Drug Abuse Reporting Program (DARP) study, which began in the late 1960s, and the Treatment Outcome Prospective Study (TOPS) of clients entering treatment in the 1970s. The work was sponsored by the National Institute on Drug Abuse (NIDA) and conducted by the National Development and Research Institute, Texas Christian University, and the University of California, Los Angeles.

The major objective of DATOS is to examine the effectiveness of drug-abuse treatment by conducting a multisite, prospective clinical and epidemiological longitudinal study of drug-abuse treatment. Effectiveness was examined by using data from 10,010 client interviews conducted from 1991 to 1993 at entry to treatment each three months, during treatment, and one year after leaving treatment. Interviews of clients at admission were supplemented with comprehensive clinical assessments of psychological, social, and physical impairments in addition to drug and alcohol dependence. Treatment outcomes were compared for clients who entered treatment with varied patterns of drug abuse and levels of psychosocial impairment.

A secondary objective was to investigate the process of drug-abuse treatment. A detailed examination was being conducted of the treatments and services available and provided to each client, how these treatments and services are delivered to the client, and how the client responds to treatment in terms of cognitive and behavioral changes.

The study population includes 1,540 clients from twenty-nine outpatient methadone programs; 2,774 clients from twenty-one long-term residential or therapeutic community programs; 2,574 clients from thirty-two outpatient drug-free programs; and 3,122 clients from fourteen short-term, inpatient, or chemical dependency programs. In addition, treatment programs from DATOS were compared with those for TOPS a decade earlier and for DARP two decades earlier in order to determine how drug-abuse treatment programs have changed and what the changes imply for the provision of effective treatment approaches and services.

The DATOS research builds and expands the knowledge generated from previous research on the effectiveness of treatment. Several events, however, have necessitated a continuing nationally based multisite study of drug-abuse treatment and treatment effectiveness. Major changes have occurred in the nation's drug-abusing population and treatment system. The OMNIBUS Recommendation Act of 1981 shifted the administration of treatment programs from the federal government to the states. The AIDS epidemic has intensified interest in drug-abuse treatment as a strategy to reduce exposure to the human immunodeficiency virus (HIV), which causes AIDS. Cocaine use rather than opioid use was the major drug problem of the late 1980s and early 1990s. Efforts to contain health-care costs may dramatically transform both the public and private treatment systems. It has therefore become necessary to update information so as to reexamine what we have learned about treatment effectiveness, and so as to augment the types of data that are available for exploring new issues about the nature, effectiveness, and costs of treatment approaches. The

research based on DATOS has been organized into four areas: (1) treatment selection, access, and utilization, (2) treatment engagement and retention, (3) addiction and treatment, and (4) applications and policy development. Details of these studies can be found in the following references as well as at the URL http://www.DATOS.org.

The initial comparison of data from the DATOS and from the TOPS shows the following about the clients in DATOS: They are older, a greater percentage of them are women, they have more years of education, more of them are married, fewer are fully employed, and a lower percentage of them report that they have considered or attempted suicide. A higher proportion of the clients on methadone are entering treatment for the first time, and the proportion of criminal-justice referrals is higher in long-term residential and outpatient drug-free programs than they are in short-term inpatient programs.

In all types of programs, cocaine abuse predominated in the early 1990s, compared to heroin abuse in the past, but the cocaine use was usually combined with extensive use of alcohol. Multiple abuse of psychotherapeutic agents has decreased, so less than 10 percent of clients report that they regularly use these agents as opposed to treatment services. Outpatient programs have fewer early dropouts, but this may reflect better screening and longer, more extensive intake processes. The influence of cost-containment measures and managed care became evident with shortened durations of treatment for short-term inpatients. Short-term inpatient programs also admit more public sector patients than in the 1980s. Early analyses from the DATOS indicate that rates of drug use toward the start of outpatient treatment are two to three times higher than those that were found in TOPS.

The early results of DATOS also show that clients entering drug treatment are a diverse group who have multiple problems. Two-thirds of the clients are men, and approximately half have previously been in treatment. Those who have health insurance that covers treatment are, by far, in the minority. Although the clients entering short-term inpatient chemical-dependency programs appear to have a higher rate of private insurance coverage (40 percent) than any other classification of clients, their rate is considerably lower than that observed among the same type of clients in the 1980s. Depending on the type of treatment, 25 to 50 percent of clients reported predatory criminal activity in the previous year, and less than 20 percent were fully employed. The clients have a variety of health problems, and many report significant psychiatric impairment. Few have received mental health services, however, and about one in every three clients report that they use emergency rooms as their primary health-care provider. Taken together, these data indicate that most clients have deficits in many areas of their lives and have multiple needs in addition to those directly related to their drug abuse (e.g., medical services and vocational needs).

Patterns of drug use vary markedly by type of treatment in DATOS clients. Although cocaine is the most frequently cited drug of abuse, most clients abuse multiple drugs and exhibit complex patterns of drug use. Frequent alcohol use is also common among many of the clients, as is weekly use of marijuana. Multiple abuse of psychotherapeutic agents is reported by less than 10 percent of clients.

Drug-treatment programs are focusing on providing drug-counseling services to meet the multiple problems of clients, but fewer specialized services, such as medical or psychological services, are being provided to meet clients' other needs. Only a third to a half of clients who report a need for medical services are receiving them, and the situation is much worse in regard to psychological, family, legal, employment, and financial services. Less than 10 percent of clients who report a need actually receive the service while they are in methadone and outpatient drug-free programs. The percentage of clients who receive specialized services other than drug counseling (e.g., medical or psychological attention) has declined dramatically since the mid-1980s. The impact of cost-containment measures and managed care is evident in the shorter stays of clients, particularly those enrolled in short-term inpatient programs.

Limited information on treatment outcomes has provided a mixed indication of the outcomes of treatment. The combination of more severe impairment and less extensive services suggests the potential for poorer outcomes. On the positive

side, clients in treatment are being retained in treatment. However, compared to earlier findings, findings from the early 1990s indicated that a higher percentage of clients were actively using drugs during the first months of treatment.

Two other studies have been included under the DATOS program of research. The Drug Abuse Treatment Outcome Study–Adolescent (DATOS–Adolescent) research study is designed to examine the effectiveness of drug-abuse treatment for adolescents through a multisite prospective longitudinal study of youth entering treatment programs that focus on adolescents. Effectiveness will be examined by using interview data from youth under eighteen supplemented by interviews with parents or guardians conducted at entry to treatment, during treatment, and one year after leaving treatment. Treatment outcome will also be assessed by using such measures as changes in the use of the primary problem drug; the use of other drugs; antisocial, delinquent, or criminal behavior; school attendance and achievement; vocational training and employment; family and social functioning; and treatment retention. A secondary objective of DATOS–Adolescent is to investigate the drug-abuse treatment that adolescents receive. A sample of thirty long-term residential, outpatient drug-free, and short-term inpatient programs will be used to accomplish these objectives. The proposed sample design will include three thousand clients.

The Early Retrospective Study of Cocaine Treatment Outcomes is an accelerated retrospective study of clients with a primary diagnosis of cocaine dependence who had been admitted to DATOS–Adult programs prior to or in the early stages of DATOS. The research will provide data about outcomes for cocaine abusers during the first year of treatment, describe the treatment received by these clients through a study of treatment process, and establish a client data base for future follow-up studies. A sample of 2,000 records for cocaine-abusing clients discharged from residential, hospital-based, and outpatient nonmethadone programs will be abstracted to obtain baseline data. A sample of 1,200 face-to-face, follow-up interviews will be completed, after twelve months of treatment, with the discharged clients whose records were reviewed during the record-abstraction phase of the project.

Data analyses of the project will be targeted at describing the posttreatment outcomes for cocaine abusers by detailing their treatment experiences and investigating their posttreatment experiences. This description will include the type, intensity, and duration of services received and an examination of the interrelationships between client and treatment characteristics and posttreatment outcomes. Along with cocaine use, other outcomes that will be considered include the use of drugs other than cocaine, economic functioning, illegal activities, and psychological status. Analytic methods will include univariate and descriptive statistics as well as multivariate methods. The collection of follow-up data for this retrospective study will be conducted simultaneously with the collection of data for the twelve-month follow-up of DATOS clients. A close coordination with the DATOS–Adult is designed to permit comparison across studies.

See also **Drug Abuse Reporting Program (DARP); Methadone Maintenance Programs; Opioid Dependence: Course of the Disorder Over Time; Treatment: A History of Treatment in the United States; Treatment Outcome Prospective Study (TOPS).**

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ROBERT HUBBARD
REVISED BY DWAYNE SIMPSON (2001)

DRUG ABUSE WARNING NETWORK (DAWN). The Drug Abuse Warning Network (DAWN) provides information on some of the medical consequences of substance use, misuse, and abuse that manifest in visits to hospital emergency departments. DAWN records substances associated with drug-related emergency department visits; provides a means for monitoring drug misuse and abuse patterns, trends, and the emergence of new substances; assesses some of the morbidity associated with drug misuse and abuse; and generates information for national, state, and local drug policy and program planning. DAWN is also a tool that is increasingly being used for postmarketing surveillance and risk management for the pharmaceuticals regulated by the Food and Drug Administration (FDA). DAWN is the responsibility of the Office of Applied Studies, a federal statistical unit within the Substance Abuse and Mental Health Services Administration (SAMHSA).

DAWN was established in 1972 by the U. S. Department of Justice, Drug Enforcement Administration (DEA), primarily as a surveillance system for new drugs of abuse. In 1980 responsibility for DAWN was transferred to the U.S. Department of Health and Human Services (HHS). At HHS, DAWN was initially managed by the National Institute on Drug Abuse (NIDA) and, more recently, by the Office of Applied Studies at SAMHSA.

At its outset the DAWN system included inpatient units of non-federal, short-term, general hospitals; emergency departments of such hospitals; county medical examiners or coroners; student health centers; and crisis intervention centers not directly affiliated with colleges and universities. Initially, data were collected in selected metropolitan areas in each of thirteen DEA regions. Later in its development, DAWN concentrated its focus on emergency departments and medical examiners/coroners. Additionally, a probability sample of hospitals capable of producing estimates for 21 metropolitan areas and estimates for the coterminous United States was instituted for the first time after NIDA became responsible for DAWN operations. Statistical estimates of the number of hospital emergencies in the metropolitan areas or across the nation were not available from 1972 to 1987.

Beginning in 1988 DAWN data were collected from a representative sample of eligible hospitals in 21 metropolitan areas. A sample of hospitals from outside the 21 metropolitan areas was used to supplement the metropolitan areas and enabled the production of estimates for the coterminous United States as well as the 21 metropolitan areas.

Even with annual sample maintenance, such factors as changes in the hospital industry, the health care system as a whole, and major shifts in the population of the United States resulted in a need to consider changes to the sample and other features of DAWN that had remained static since its inception in 1972. As a result OAS/SAMHSA launched a two-year evaluation of DAWN's features, which resulted in a plan for a comprehensive new design.

The new data collection protocol was introduced for DAWN in 2003. This new design addressed many long-standing limitations associated with DAWN data. Because virtually every feature of DAWN changed with the redesign, data from 2004 and beyond are not comparable to data from 2002 and prior years. Data from 2003 represent a transition year that is not comparable to prior or subsequent years.

Today, DAWN relies on a national probability sample of non-federal, short-stay, general hospitals that operate 24-hour emergency departments. Hospitals are oversampled in selected metropolitan areas and divisions, and a remainder sample covers hospitals in the rest of the United States. Based on data from sampled units, national estimates of drug-related emergency department visits for the United States are produced annually.

DAWN estimates for 2006 are based on a sample of 544 eligible hospitals, with 160 (28% to 70%) responding in oversample areas and 45 (23%) responding in the remainder area. Estimates reflect adjustments for the stratified sample design, unit nonresponse, and nonresponse within a facility. Whether an oversample area stands alone in the national estimate depends on its response rate and the potential for nonresponse bias. At this time, comparisons over time are available only for 2004, 2005, and 2006.

In addition, authorized users in DAWN member hospitals; federal, state, and local public health agencies, including SAMHSA and the FDA; and

New DAWN (began 2003)	Old DAWN (ended 2002)
Cases reported to DAWN	
All types of drug-related ED visits	ED visits related to drug abuse only
Simple case criteria: Any ED visit related to recent drug use	Complex case criteria: ED visits related to drug abuse, defined as the use of an illicit drug or the non-medical use of a licit drug for one of the following purposes: • Suicide attempt or gesture • Dependence • To achieve psychic effects
Current or recent drug use	Drug abuse at any time • Current or recent drug abuse • Past (history of) drug abuse
Patient's intent is not considered	Patient's intent to abuse a drug was key
Patients of any age	Patients age 6 to 97
Eight case types: • Suicide attempt • Seeking detox • Alcohol only (age $<$ 21) • Adverse reaction (to pharmaceuticals) • Overmedication • Malicious poisoning • Accidental ingestion • Other (any case not categorized above)	One case type with three subcategories: • Suicide attempt or gesture • Seeking detox • Other drug abuse
Drugs reported to DAWN	
Only those drugs related to the ED visit	Any drug
All types of drugs: • Illicit drugs • Prescription and over-the-counter medications • Dietary supplements • Non-phamaceutical inhalants	Same as new DAWN
Maximum of six drugs, plus alcohol	Maximum of four drugs, plus alcohol
"Alcohol-in-combination" for any case; "Alcohol only" for patients age $<$ 21	"Alcohol-in-combination" (alcohol with another reportable drug) only
Current medications reported only if related to the visit	Current medications reported, even if unrelated to the visit
Other data items	
Whether each drug was confirmed by toxicology	No information about laboratory confirmation
Information about health: • Chief complaints • Diagnoses	No information about health
Expanded categories for patient disposition: • Three categories for treated and released • Five categories for patients admitted to the hospital	Limited categories for patient disposition: • One category for treated and released • One category for patients admitted to the hospital
Form and source of drug are not collected	Form and source of drug
Six categories for route of administration	Seven categories for route of administration

Table 1. Comparison of major features, new DAWN versus old DAWN. (Source: Drug Abguse Warning Network, Office of Applied Studies, Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services, 2004.)
ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

New DAWN (began 2003)	Old DAWN (ended 2002)
Other changes	
Case finding by retrospective review of medical charts for all patients treated in the ED	Screening methods with limited chart review
Rigorous reporter training and quality assurance	Limited oversight
Performance feedback to hospitals and reporters	Limited feedback
Sample of hospitals	
Sample of hospitals representing the complete United States	Sample of hospitals representing the coterminous United States (48 States)
Eligible hospitals: Short-term, general, non-Federal hospitals operating 24-hour EDs	Same as new DAWN
Complete National estimates based on: • Oversampling in designated metropolitan areas • "Supplementary sample" representing hospitals outside those areas in all 50 States and the District of Columbia	Estimates for coterminous United States based on: • Oversampling in 21 metropolitan areas • "National panel" sample representing hospitals outside those areas in the 48 States and the District of Columbia
Metropolitan areas represented: • Boundary definitions based on the 2000 census • Expansion to additional areas planned	Metropolitan areas represented: • Boundary definitions based on the 1980 census • Oversampling in 21 areas

ED = emergency department.

Table 1 (continued). Comparison of major features, new DAWN versus old DAWN. (Source: Drug Abuse Warning Network, Office of Applied Studies, Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services, 2004.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

pharmaceutical firms receive access to the raw DAWN case data, in de-identified form, as the DAWN cases are submitted. This surveillance of sentinel events is possible through a secure, Internet-based query system called DAWN *Live!*

To collect the data, each hospital emergency department that participates in DAWN has one or more reporters who review emergency department medical records retrospectively to find DAWN cases. Cases reported to DAWN include emergency department visits caused by or related to drug use for patients of any age. (From 1972 to 2002 DAWN used case criteria that depended on the patient's intent to abuse a drug. Upon evaluation, the case criteria and case finding methods were revamped with the redesign.) The drug use must be recent; chronic effects and history of drug abuse are not reportable. Visits related to drugs used for therapeutic purposes, as well as drug misuse and abuse, are all included.

For each reportable visit the demographic, visit, and drug characteristics are abstracted from the medical record. Each DAWN visit is classified into one of eight case types:

1. Drug-related suicide attempt
2. Seeker of detoxification or substance abuse treatment services
3. Underage alcohol use (with no other drug involved)
4. Adverse reactions to pharmaceuticals taken as prescribed
5. Overmedication when the dose of a prescription or over-the-counter medication or dietary supplement was exceeded
6. Malicious poisonings
7. Accidental ingestions when a drug was used accidentally or unknowingly
8. All others, including explicit drug abuse

This classification and the drugs reported to DAWN are used to derive analytic subgroups (e.g., for visits involving illicit drug use, alcohol use, or nonmedical use of pharmaceuticals) for a variety of purposes and audiences. Other data items

characterize drug-related visits in terms of diagnoses or disposition.

DAWN captures very detailed drug information. As many as 16 drugs, plus alcohol, are reported for each DAWN case. Drug-related emergency department visits often include multiple drugs—on average 1.6 drugs per visit. For adults, alcohol is reportable only when present with another reportable drug; for minors, alcohol is always reportable. Drug information is captured at the level of detail present in the medical record. The same drug may be reported to DAWN by brand, generic, chemical, street, or nonspecific name, depending on the completeness and specificity of information in the medical record. Training and automated rules prompt DAWN reporters to use all available documentation in the medical chart to record drugs by their most specific names (e.g., OxyContin, when documented as such, instead of oxycodone), not to record the same drug by different names (e.g., heroin and opiates), and to exclude current medications unrelated to the visit. Estimates are published at the generic level (e.g., acetaminophen-hydrocodone), for specific ingredients (e.g., dextromethorphan), or by drug category (e.g., opiates/opioids, benzodiazepines). Estimates attributed to particular brand or trade names (e.g., Concerta) are generally not published.

Because data for DAWN are extracted from a retrospective review of medical records, no patients or health care providers are interviewed. Health care settings within the hospital but outside of the emergency department, or emergency facilities outside of hospitals, are not covered. Laboratory findings to detect the presence of a drug are not recorded for DAWN cases, although each drug report has an associated indicator for whether the drug was confirmed by toxicology testing. Only the patient's own drug use is considered; a patient's intent to misuse or abuse a drug is not a factor in the DAWN case determination, and source of the drug is not captured because it is so rarely available in medical records. Repeat visits by the same individual cannot be linked together. Visits due to chronic conditions associated with a history of drug abuse are explicitly excluded. While DAWN does not collect direct identifiers, such as patient name, the content of the case data does render the data individually identifiable, and individually identifiable data are protected by federal law from disclosure without consent.

Drug-related emergency department visits may not accurately reflect the level or type of drug abuse in the population as a whole. Therefore, DAWN should not be interpreted as measuring the prevalence of drug abuse in the population. For example, the availability of health insurance and/or other sources of care may influence whether an individual seeks care in an emergency department. Purity of the drug, experience with a particular drug, or other factors related to the physiological effects of drugs may affect whether a condition gives rise to an emergency department visit.

DAWN also collects data on drug-related deaths reviewed by medical examiners and coroners (ME/Cs) in selected metropolitan areas and selected states. The death investigation jurisdictions that participate in DAWN do not constitute a statistical sample nor is every jurisdiction within a metropolitan area necessarily a participant. As a result, extrapolation of drug-related deaths to the nation as a whole is not possible, and metropolitan area totals are only possible if all jurisdictions within the area participate. The number of jurisdictions that participate in DAWN varies from year to year. In 2003, the last year for which mortality data were published, 122 jurisdictions in 35 metropolitan areas and 126 jurisdictions constituting six states participated in DAWN. The case criteria and data collection procedures for drug-related deaths mirror those used in emergency departments. Causes and manner of death are captured in lieu of case type and diagnoses.

See also **Abuse Liability of Drugs: Testing in Humans; Accidents and Injuries from Drugs; Drug Interactions and Alcohol; Epidemiology of Drug Abuse; National Survey on Drug Use and Health (NSDUH); U.S. Government Agencies: National Institute on Drug Abuse (NIDA); U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA).**

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DRUG COURTS. Drug courts emerged as a method for responding to America's drug problems at a time when health, treatment, and justice systems were overwhelmed by the drug epidemics of the 1980s. The dramatic increase in the availability of cocaine and, later, crack cocaine, particularly in America's cities, translated into a new challenge for the criminal justice system that was already at its limits. The volume of court cases exploded, pushing the judicial process to its limits and threatening traditional modes of managing the criminal caseload. Worse, the huge wave of arrests of drug offenders beginning in and accelerating during the 1980s found a correctional system of local jails and state prisons in many locations in the nation that was already chronically overcrowded. With little room in prisons for the new arrestees, institutional crowding was exacerbated and the processing of criminal cases was slowed, causing backlogs in the courts and a wide range of problems for the justice system as a whole.

In 1989 drug courts began experimentally as an answer to mounting drug-related arrests and to the undeniable fact that incarceration alone did not halt the drug-crime cycle (Sanford & Arrigo, 2005). The first drug court in the United States went into operation in Miami under the supervision of Judge Stanley Goldstein, the nation's first drug court judge. Since the breakthrough efforts of the Miami justice leaders, the growth of drug courts in the United States has been extraordinary. In the Bureau of Justice Assistance [BJA] and National Drug Court Institute's annual report titled *Painting the Current Picture: A National Report Card on Drug Courts and Other Problem Solving Courts*, statistics indicate that in 2007 there were 2,147 problem solving-courts in operation in the United States. Of these, there were 1,174 adult drug courts, 455 juvenile drug courts, 301 family dependency courts, 110 DWI (Driving While Under the Influence) courts, 24 reentry courts (an approach to improving offenders returning to their communities from prison), 72 Tribal courts (a court administered through self-government of an American Indian tribe on a reservation and having federally prescribed jurisdiction over custody and adoption cases involving tribal children, criminal jurisdiction over offenses committed on tribal lands by members of the tribe, and broader civil jurisdiction over claims between tribe members and nonmembers), six campus drug courts, and five Federal District drug courts. Furthermore, in the early twenty-first century, England and Wales have introduced drug courts, community courts, and domestic-violence courts; and other countries such as South Africa, Canada, Scotland, New Zealand, Australia, Ireland, Bermuda, and Jamaica have erected other problem-solving courts.

Drug courts represent the coordinated efforts of justice and treatment professionals to actively intervene and break the cycle of substance abuse, addiction, and crime. As an alternative to less effective interventions, drug courts quickly identify substance-abusing offenders and place them under ongoing judicial monitoring and community supervision coupled with effective, long-term treatment services (Huddleston, Marlow, & Casebolt, 2008). The foundation of the drug court model lies in its underlying values, philosophical outlook, and the central role it assigns to the judge as it incorporates a mix of values with a decided shift toward treatment and restoration of offenders to the community. The mix also includes deterrent and desert values.

The therapeutic activities associated with the treatment-oriented drug court occur in a "theater in the square," the square representing not only the architectural features of the physical courtroom

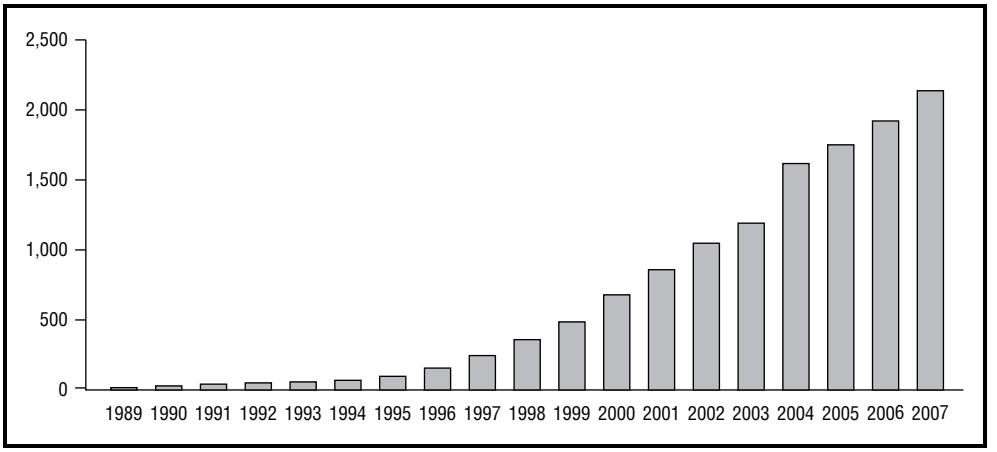

Figure 1. Number of drug courts in the United States, 1989–2007. (Adapted from National Drug Court Institute, January 2008.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

but also the boundaries imposed by the criminal process. Led and closely supervised by the judge, the drug court operates in the context of the criminal process and, therefore, differs notably from substance abuse treatment provided to addicted citizens in civilian contexts outside of the justice system. Within those judge-enforced boundaries marking the criminal process, however, the drug court model created a new working relationship between the criminal court and health, treatment, and related services that adapts the criminal process to the needs of treatment and an understanding of addiction. The drug court seeks to resolve the apparently contradictory aims of the typically punitive justice process and the more supportive treatment process.

Prior to the implementation of drug courts, the criminal justice system did not have the capacity to identify offenders with serious drug problems. As a result, the likelihood of offenders being placed in treatment was poor and depended on their being convicted and, usually, sentenced to probation. (Only in rare cases would incarceration include drug treatment.) Before the inception of drug courts, drug treatment has also been available for less serious offenses but has not demonstrated significant impact. From a judicial perspective, however, the court's typical involvement in substance abuse treatment was to order or refer offenders to treatment, if such treatment was recommended by probation staff at the pre-sentence stage. The judge in such cases would have little other involvement in the treatment process, except to set treatment as a condition of probation, and, later, to hear allegations of noncompliance at revocation hearings. By keeping a judicial distance from the treatment process, judges deferred to the expertise and practices of treatment providers and probation agencies whose responsibilities were to manage and monitor the treatment process.

Drug courts were established to reinvent a helping justice role, similar to the one formerly played by probation services, but this time entrusted to the authority of the criminal court judge and occurring at an earlier stage. The justice and treatment systems working together in drug courts can achieve the goal of providing an intensive regimen of substance abuse treatment, case management, drug testing, and probation supervision along with regularly scheduled status hearings before a judge with specialized expertise in the drug court model (Huddleston, Marlow & Casebolt, 2008; Fox & Huddleston, 2003). In addition to these general elements of the treatment-oriented philosophy, the central judicial role, and new criminal court-treatment relationship, drug courts are characterized by other distinguishing elements. The Drug Court Program Office of the U.S. Department of Justice sponsored an initiative by the National Association of Drug Court Professionals (NADCP) to identify key components of drug courts. The ten components identified by NADCP

and adopted as a standard by the Justice Department in reviewing grant applications include integration of treatment and case processing; use of a non-adversarial approach that also respects due process and public safety; early identification and enrollment of participants; provision of a continuum of treatment services; provision of drug testing; inclusion of court responses to performance in treatment; hands-on judicial supervision of treatment; monitoring and evaluation; continuing interdisciplinary education; and, forging partnerships between the court and other criminal justice, health, social service agencies, and the community.

Prior to the NADCP identification of key components of drug courts for constructing standards, a working typology of drug courts identified eight critical dimensions of the drug court innovation mainly for the purposes of evaluation. These include addressing the target problems drug courts were designed to handle; targeting specific criminal justice populations to enroll in treatment; employing mechanisms to identify and evaluate court treatment candidates; modifying the traditional court process, structure, and content of the treatment delivered to substance abusing offenders; altering the methods employed in the drug courts to encourage positive and discourage negative behavior by participants (including the use of sanctions and incentives); measuring the productivity of the courts (in terms of outcomes such as reduced substance abuse and criminal behavior); and assessing the extent of system-wide support in and outside criminal justice and health systems.

Drug courts combine the goals of justice and treatment in a pragmatic effort to curtail substance abuse, dependence and crime. AP IMAGES

ADULT DRUG AND DWI COURTS

Drug court evaluations boast some impressive outcomes (Sanford & Arrigo, 2005). Research verifies that no other justice intervention can rival the results produced by drug courts. According to more than a decade of research, drug courts significantly improve substance abuse treatment outcomes, substantially reduce crime, and produce greater cost benefits than any other justice strategy. As such, scientists from the Treatment Research Institute at the University of Pennsylvania reported in 2003, drug courts outperformed virtually all other strategies used with drug-involved offenders (Huddleston, Marlow & Casebolt, 2008; NADCP, 2008). In February 2005 the U.S. Government Accountability Office (GAO, 2005) issued its third comprehensive report on the effects of adult criminal drug courts. At the time results of 23 program evaluations confirmed that drug courts significantly reduced crime. In addition, although up-front costs were somewhat higher for drug courts than for standard probation, drug courts were determined to be more cost-effective because they avoided expenditures related to law enforcement efforts, judicial case-processing, and victimization resulting from future criminal activity. In the ensuing years researchers continued to uncover definitive evidence for the efficacy and cost-effectiveness of drug courts (NADCP, 2008). In 2005 Sanford & Arrigo reported the findings from a two-year follow-up that indicated the re-arrest rate for graduates was 19 percent compared to 53 percent for non-graduates. In another evaluation, findings indicated that 20 percent of the graduating participants recidivated, or relapsed, within 12 months, compared to 51 percent for non-participants. Drug-related arrest rates decreased, with drug court graduates being arrested significantly less (13%) than non-drug court participants (30%) within the same period.

The most rigorous and conservative measurement of the effect of any program is derived from what scientists call *meta-analysis.* This involves statistically averaging the effects of a program over dozens of research studies. Five independent meta-analyses concluded that adult drug courts significantly reduce crime by an average of 8 to 26 percent. Importantly, because these figures reflect *average* effects, they also include drug court programs that were new or were

not well implemented. Well-administered drug courts reduced crime rates by as much as 35 percent (NADCP, 2008).

Numerous drug court and DWI court program evaluations have reported similar findings. In most instances, re-arrest rates for drug court and DWI court participants were approximately 15 percent lower than for comparable individuals on probation or adjudication as usual. In a nationally representative sample of more than 2,000 graduates from 95 different drug courts, the average re-arrest rate was only 16 percent in the first year after leaving the program and 27 percent after the second year (NADCP, 2008; Roman et al., 2003). This compares highly favorably to typical recidivism rates on conventional probation, in which roughly 46 percent of offenders commit a new offense, and more than 60 percent commit a probation violation one year after completing probation supervision (Langan & Cunniff, 1992). A recent study of nine drug courts in California found that re-arrest rates over a four-year period were 29 percent for drug court participants (and only 17% for drug court graduates) as compared to 41 percent for similar drug offenders who did not participate in drug court (NADCP 2008, Carey et al., 2006). Another study of four adult drug courts in Suffolk County, MA, found that drug court participants were 13 percent less likely to be re-arrested, 34 percent less likely to be re-convicted, and 24 percent less likely to be re-incarcerated than probationers who had been carefully matched to the drug court participants using sophisticated *propensity score* analyses (NADCP 2008; Rhodes et al., 2006). A 2007 three-county evaluation of courts in Michigan found that DWI court participants were substantially less likely than comparable DWI offenders sentenced to probation to be arrested for a new DWI offense or any new criminal offense within two years of entering the programs. Participants in the DWI courts also averaged fewer re-offenses and remained arrest-free for significantly longer periods of time after leaving the programs (NADCP, 2008; Michigan State Court Administrative Office & NPC Research, 2007).

JUVENILE DRUG COURTS

The total number of criminal offenses for both juveniles and adults decreased between 1994 and 2003, but drug abuse violations increased by about 22 percent (FBI, 2003). For juveniles, specifically, drug abuse violations increased by almost 19 percent (FBI, 2003). This occurred while incarceration of juvenile drug offenders declined. According to figures from the Office of Juvenile Justice and Delinquency Prevention (OJJDP) *Census of Juveniles in Residential Placement*, detention of juveniles for drug offenses decreased by 12 percent between 1997 and 2003. This decline in incarceration for drug offenses corresponds with the increase in drug courts and an increased focus on treatment and rehabilitation.

In the mid-1990s a number of innovative jurisdictions started drug court dockets in response to juvenile offenders' cycling through courts that were ill-equipped to intervene successfully (Bureau of Justice Assistance, 2003). Because the drug court model was consistent with the original intent of juvenile courts to rehabilitate offenders and strengthen families, the drug court model was adopted without hesitation.

Juvenile drug courts were designed using the core principles of the adult drug courts, which are to assess, to refer for treatment, to monitor closely treatment progress using judicial oversight, and to shape behaviors by responding swiftly and appropriately. The goals of the juvenile drug court were to: (a) provide immediate intervention, treatment, and structure in the lives of juveniles through ongoing, active oversight and monitoring by the drug court judge; (b) improve juveniles' level of functioning in their environment, address problems that may be contributing to their use of drugs, and develop/strengthen their ability to lead crime- and drug-free lives; (c) provide juveniles with skills to aid them in leading productive substance-free and crime-free lives—including skills that relate to their educational development, sense of self-worth, and capacity to develop positive attitudes; (d) strengthen families of drug-involved youth by improving their capability to provide structure and guidance to their children; and (e) promote accountability of both juvenile offenders and those who provide services to them (Bureau of Justice Assistance, 2003).

Since the early twenty-first century, the field has learned that drug court programs for youth must incorporate individually tailored and developmentally appropriate, comprehensive treatments that

Due process	Drug court
1. Event oriented, i.e., did a certain crime happen as alleged: Historically, this is the jurisprudential link between the criminal courts and the community.	1. Process oriented, i.e., does the offender have a drug/alcohol addiction and can treatment benefit the offender? This type of process is considered in far more limited types of criminal charges.
2. Offense-specific	2. Behavior-specific
3. The determination of guilt and imposition of sentence is essentially the end of the criminal law process.	3. The determination of addiction and referral to drug court is essentially the beginning of the process.
4. The process is identical for all equally accused persons. Quite often, punishment is mandated to be identical as well. The offender's family is rarely considered in this process.	4. The offender is central to the process and quite often the treatment is individualized. The offender's family is viewed as an ingredient in the overall treatment decisions.
5. Judicial interaction exists only with the representatives of the parties.	5. Judicial interaction exists directly with the offender.
6. Responsibility equals atonement and punishment. The relationship of the offender to the community is one where, as a result of adjudication of guilt, the offender is removed from or placed in a condition that protects or shields the community from the offender.	6. Responsibility equals behavioral changes leading to restoration of mental and spiritual health. The offender is viewed as a part of the community. As the offender will generally be treated while an outpatient in the community, behavioral change is designed to reduce conflict by reducing addictive behavior.
7. When there is post adjudication monitoring, it is generally designed to uncover violations and therefore done primarily for enforcement of probation terms.	7. There is always extensive post adjudication monitoring. It is always designed to reinforce treatment.
8. The judge is neutral agent among various competitors.	8. The judge is an active participant in a partnership between the offender, the treatment providers, and the court.
9. The legal history supporting this system is approximately 400–years old; change is difficult.	9. The legal history that supports this system is 10–years old; change is relatively easy.

Table 1. Comparison between drug court models and standard criminal law due process courts. (Source: Bureau of Justice Assistance, U.S. Department of Justice.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

draw on strengths while simultaneously addressing the needs of participants and their families (Bureau of Justice Assistance, 2003). To formalize the program components and standardize measures of success of these courts across the nation, in 2003 the U.S. Department of Justice, Bureau of Justice Assistance [BJA] established 16 strategies for jurisdictions to use as a guide when planning and implementing their juvenile drug courts. They are (a) collaborative planning; (b) teamwork; (c) clearly defined target population and eligibility criteria; (d) judicial involvement and supervision; (e) monitoring and evaluation; (f) community partnerships; (g) comprehensive treatment planning; (h) developmentally appropriate services; (i) gender-appropriate services; (j) cultural competence; (k) focus on strengths; (l) family engagement; (m) educational linkages; (n) drug testing; (o) goal-oriented incentives and sanctions; and (p) confidentiality.

Although there are common elements shared by most drug courts, proliferation of the drug court model is not explained by the wholesale adoption of a fixed, cookie-cutter approach in the many jurisdictions across the nation. Therefore, to sustain continued outcome success, existing and new partners to the drug court and other problem-solving court efforts must maintain a clear vision of what they want to achieve by establishing defined goals that are tailored to unique jurisdictional characteristics.

See also **Adolescents and Drug Use; Crime and Drugs; Criminal Justice System, Treatment in the; Prevention, Education and; Treatment, Specialty Approaches to: Adolescents.**

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DRUG INTERACTION AND THE BRAIN. When two or more drugs are taken at the same time complex interactions may occur. Drugs can interact to change biological functions within the body through pharmacokinetic or pharmacodynamic mechanisms or through their combined toxic effects. Changes in the pharmacokinetic properties of a drug can include changes in absorption, distribution, metabolism, and excretion of the drug, and each of these can affect blood and plasma concentrations and, ultimately, brain levels of the drug. Although a change in the speed at which a drug reaches the bloodstream is rarely clinically relevant, a change in the amount of drug absorbed can be important, because this can lead to changes in the plasma levels of the drug, which can influence the amount of drug that reaches the brain.

The distribution of a drug throughout the body can be affected by changes in the binding of the drug to proteins in the bloodstream or by displacing the drug from tissue binding sites, both of which can affect the plasma concentration of the

drug and potentially affect the amount of drug that reaches the brain. Drug metabolism can be either stimulated or inhibited, resulting in decreased or increased plasma concentrations of the drug, respectively. The stimulation (induction) of drug-metabolizing enzymes in the liver can be produced by drugs such as the barbiturates, but a week or more is often required before maximal effects on drug metabolism are observed. As drug metabolism increases, the amount of drug available to enter the brain decreases.

The inhibition of drug metabolism often occurs much more rapidly than the stimulation, usually as soon as a sufficient concentration of the metabolic inhibitor is achieved, which results in increased plasma and brain concentrations of the drug. The renal (kidney) excretion of drugs that are weak acids or weak bases can be influenced by drugs that alter urinary pH to change the reabsorption of the drug from urine into the kidney. The active secretion of the drug into the urine can also be affected. Both processes can ultimately affect the plasma and subsequent brain concentrations of the drug. Pharmacodynamic mechanisms can either enhance or reduce the response of a given drug. For example, if two drugs are agonists for the same receptor site—diazepam (Valium) and chlordiazepoxide (Librium) for benzodiazepine receptor-binding sites—then an additive biological response is likely to occur unless a maximum response is already present. If, however, an agonist competes with an antagonist for the same binding site (e.g., see morphine and naloxone in opioids, discussed below), then a decreased biological response is likely.

Enhanced or diminished biological responses can be observed even if the drugs do not interact with the same receptor-binding sites. In this case, the net effect is the sum of the pharmacological properties of the drugs. For example, if two drugs share a similar biological response (e.g., central nervous system depression) even though they produce their effects at different sites, then the concurrent ingestion of both drugs can result in an enhanced depression of the central nervous system (see the alcohol [ethanol] and Valium discussion below). Finally, the concurrent ingestion of two or more drugs, each with toxic effects on the same organ system, can increase the chance for extensive organ damage.

DEPRESSANTS

Alcohol (Ethanol) and Valium. Reactions that are additive (combined) or synergistic (cooperative effects greater than the sum of the independent effects of the drugs taken alone) are common side effects that result from the consumption of two or more drugs with similar pharmacological properties. For example, although alcohol (ethanol) is considered by many to be a stimulant drug because, typically, it releases an individual's latent behavioral inhibitions (i.e., it produces disinhibition), alcohol actually produces a powerful depression of the central nervous system similar to that seen with general anesthetics. The subsequent impairment of muscular coordination and judgment associated with alcohol intoxication can be enhanced by the concurrent administration of other central nervous system depressants. Often, Valium or Librium (benzodiazepines that are considered relatively safe drugs) may be purposely ingested along with ethanol in an attempt to "feel drunk" faster or more easily. Since ethanol actually increases the absorption of benzodiazepines, and also enhances the depression of the central nervous system, the potential toxic side effects of the two drugs are augmented. Ethanol is often a common contributor to benzodiazepine-induced coma as well as to benzodiazepine-related deaths, demonstrating that interactions of these drugs with alcohol can be especially serious. Furthermore, the combination of alcohol with the sedative-hypnotic barbiturates (e.g., pentobarbital, secobarbital) can also produce a severe depression of the central nervous system, with decreased respiration. The intentional ingestion of ethanol and secobarbital (or Valium) is a relatively common means of suicide.

Alcohol (Ethanol) and Opioids. Alcohol can also enhance the respiratory depression, sedation, and hypotensive effects of morphine and related opioid drugs. Therefore, the concurrent ingestion of the legal and socially acceptable drug ethanol with other sedatives, hypnotics, anticonvulsants, antidepressants, antianxiety drugs, or with an analgesic agent (such as morphine) can result in serious and potentially fatal drug interactions through a potentiation of the depressant effects of these drugs on the central nervous system. Since the 1960s, a significant number of musicians, actors, and other high-profile personalities have either accidentally or intentionally overdosed from a combination of

alcohol and other central nervous system depressants. A few notable examples include actress Marilyn Monroe, musicians Jimi Hendrix, Janis Joplin, Jim Morrison, Keith Moon, and John Bonham.

STIMULANTS

Stimulants and Toxic Effects. Synergistic toxic effects are also often obscured with other classes of drugs. For example, the concurrent ingestion of central nervous system stimulants (e.g., amphetamine, cocaine, caffeine) can also produce additive side effects, especially with respect to toxic reactions involving the heart and cardiovascular system. These toxic reactions are often manifested as an irregular heartbeat, stroke, heart attack, or even death. Drugs with apparently different mechanisms of action can result in dangerous and unexpected synergistic side effects with fatal consequences. For example, some amphetamine and cocaine users often attempt to self-medicate their feelings of "overamp," or the excessive stimulant high resulting from prolonged central nervous system stimulation, through the concurrent administration of central nervous system depressants such as alcohol, barbiturates, or heroin (i.e., a "speedball"). The rationale behind this potentially dangerous practice is that a few beers, a Quaalude, or perhaps a shot of heroin will help the individual "mellow out" for a while before inducing a stimulant high again. High doses of cocaine or amphetamine can, however, result in respiratory depression from actions on the medullary respiratory center. Therefore, the concurrent ingestion of a central nervous system stimulant (e.g., cocaine) with a depressant (e.g., heroin) can result in increased toxicity or death from the enhanced respiratory depression produced by the combination of the two drugs. The most well-known casualty from this type of pharmacological practice was comedian John Belushi.

CLINICAL USES

The principles of drug interactions can be used clinically for the treatment of acute intoxication and for withdrawal—by transforming, reducing, or blocking the pharmacological properties and/or the toxic effects of drugs used and abused for nonmedical purposes. Although these interactions often involve a competition with the abused drug for similar central nervous system receptor sites, other mechanisms are also clinically relevant.

Disulfiram and Alcohol (Ethanol). One such nonreceptor-mediated interaction involves disulfiram (Antabuse) and ethanol (alcohol). Since an ethanol-receptor site has not yet been conclusively identified, specific receptor agonists and antagonists are not yet available for the treatment of ethanol intoxication, withdrawal, and abstinence (as they are for opioids). Disulfiram is sometimes used in the treatment of chronic alcoholism, although the drug does not cure alcoholism; rather, it interacts with ethanol in such a way that it helps to strengthen an individual's desire to stop drinking. Although disulfiram by itself is relatively nontoxic, it significantly alters the intermediate metabolism of ethanol, resulting in a five- to tenfold increase in plasma acetaldehyde concentrations. This acetaldehyde syndrome results in vasodilatation (dilation of blood vessels), headache, difficulty breathing, nausea, vomiting, sweating, faintness, weakness, and vertigo. All of these reactions are obviously unpleasant, especially at the same time, thus well worth avoiding. The acetaldehyde syndrome therefore helps to persuade alcoholics to remain abstinent, since they realize that they cannot drink ethanol for at least three or four days after taking disulfiram. The consumption of even small or moderate amounts of ethanol following disulfiram pretreatment can result in extremely unpleasant drug interactions through the acetaldehyde syndrome.

Opioids. Drug interactions involving opioids (morphine-like drugs) and opioid receptors are classic examples of how knowledge of the molecular mechanisms of the actions of a class of drugs can assist in the treatment of acute intoxication, withdrawal, and/or abstinence. Naloxone, the opioid-receptor antagonist, can be used as a diagnostic aid in emergency rooms. In the case of a comatose patient with unknown medical history, the intravenous administration of naloxone can provide information on whether or not the coma is the result of an opioid overdose. The antagonist competes with the agonist (usually heroin or morphine) for the opioid-receptor sites, displacing the agonist from the binding sites to reverse the symptoms of an overdose effectively and rapidly. Continued naloxone therapy and supportive treatment are often still necessary.

If, however, naloxone is administered to an individual dependent on opioids but not in a coma, a severe withdrawal syndrome develops within a few minutes and peaks after about thirty minutes. Depending on the individual, such precipitated withdrawal can be more severe than that following the abrupt withdrawal of the opioid-receptor agonist (e.g., heroin). In the former instance, the binding of the agonist to opioid receptors is suddenly inhibited by the presence of the antagonist (e.g., naloxone); even relatively large doses of the agonist (e.g., heroin) cannot effectively overcome the binding of the antagonist. Quite the contrary, respiratory depression can develop if higher doses of the agonist are administered. Therefore, opioid-receptor antagonists are not recommended for the pharmacological treatment of opioid withdrawal. Rather, longer acting, less potent, opioid receptor-agonists, such as methadone, are more commonly prescribed.

Methadone. The symptoms associated with methadone withdrawal are milder, although more protracted, than those observed with morphine or heroin. Therefore, methadone therapy can be gradually discontinued in some heroin-dependent people. If the patient refuses to withdraw from methadone, the person can be maintained on methadone relatively indefinitely. Tolerance develops to some of the pharmacological effects of methadone, including any reinforcing or rewarding effects (e.g., the euphoria or "high"). Therefore, the patient cannot attain the same magnitude of euphoria with continued methadone therapy, although the symptoms associated with opioid withdrawal will be prevented or attenuated. Cross-tolerance also develops to other opioid drugs, so the patient will not feel the same high if heroin is again used on the street.

This type of maintenance program makes those who are heroin dependent more likely to accept other psychiatric or rehabilitative therapy. It also reduces the possibility that methadone patients will continue to seek heroin or morphine outside the clinic. In this way, the principles of drug interactions involving opioid receptors in the central nervous system have helped to stabilize treatment strategies for opioid withdrawal and abstinence.

See also **Accidents and Injuries from Drugs; Complications: Neurological; Drug Abuse Warning Network (DAWN).**

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DRUG INTERACTIONS AND ALCOHOL. The term *alcohol-drug interaction* refers to the possibility that alcohol may alter the intensity of the pharmacological effect of a drug, so that the overall actions of the combination of alcohol plus drug are additive, potentiated, or antagonistic. Such interactions can be divided into two broad categories—pharmacokinetic and pharmacodynamic. Pharmacokinetics are concerned

with the extent and rate of absorption of the drugs, their distribution within the body, binding to tissues, biotransformation (metabolism), and excretion. Pharmacokinetic interactions refer to the ability of alcohol to alter the plasma and tissue concentration of the drug and/or the drug metabolites, such that the effective concentration of the drug at its target site of action is significantly decreased or increased. Pharmacodynamics are concerned with the biochemical and physiological effects of drugs and their mechanisms of action. Pharmacodynamic interactions refer to the combined actions of alcohol and the drug at the target site of action, for example, binding to enzyme, receptor, carrier, or macromolecules. Pharmacodynamic interactions may occur with or without a pharmacokinetic component. For many drugs acting on the central nervous system that exhibit cross-tolerance (a similar tolerance level) with alcohol, pharmacodynamic interactions with alcohol are especially important.

Most drugs are metabolized in the liver by an enzyme system usually designated as the cytochrome P450 mixed-function oxidase system, and the liver is the principal site of many alcohol-drug pharmacokinetic interactions. Two major factors—blood flow to the liver and the activity of drug-metabolizing enzymes—strongly influence the overall metabolism of drugs. Biotransformation of drugs that are actively metabolized by liver enzymes mainly depends on the rate of delivery of the drug to the liver. These may be flow-limited drugs, where the liver can transform as much drug as it receives, or capacity-limited drugs, which have a low liver-extraction ratio—their clearance (removal from the blood) primarily depends on the rate of their metabolism by the liver.

There are a number of factors other than the drugs themselves that influence the speed and intensity of alcohol/drug interactions in the human body. These include the patient's sex, weight, age, and race; the presence or absence of food in the stomach; and history of alcohol intake. For example, the levels of alcohol dehydrogenase (ADH), a stomach enzyme that oxidizes alcohol to acetaldehyde, are lower in women than in men; lower in Asians than in Western Caucasians; and lower in alcoholics than in nonalcoholics. Elderly persons are at greater risk of alcohol/drug interactions than younger adults, because they usually take more prescription medications, are more likely to have a serious illness, and show age-related changes in the absorption and clearance of certain medications. With regard to stomach contents, food generally slows the rate of alcohol absorption. Consequently, medications that increase the rate of gastric emptying, such as erythromycin (Eryc, Ilotycin) or cisapride (Propulsid), enhance the rate of alcohol metabolism.

ALCOHOL-DRUG INTERACTIONS

Alcohol-drug interactions are complex. The consequences of using alcohol and drugs together vary with the dosage of the drug; the amount of alcohol consumed; the mode of administering the drug (oral, intravenous, intramuscular, etc.); and the nature of the drug (anticonvulsant, vasodilator, analgesic, etc.). The alcohol may alter the effects of the drug; the drug may change the effects of alcohol; or both may occur.

Alcohol-drug interactions are most important with drugs that have a steep dose-response curve and a small therapeutic ratio—so that small quantitative changes at the target site of action lead to significant changes in drug action. In alcoholics, changes in susceptibility to drugs are due to changes in their rates of metabolism (pharmacokinetics) and the adaptive and synergistic effects on their organs, such as the central nervous system (pharmacodynamics). The clinical interactions of alcohol and drugs often appear paradoxical: Sensitivity to many drugs, especially sedatives and tranquilizers, is strikingly increased when alcohol is present at the same time; however, alcoholics, when abstinent, are tolerant to many drugs. These acute and chronic actions of alcohol have been attributed, respectively, to additive and adaptive responses in the central nervous system (pharmacodynamic interactions).

It is now recognized that alcohol can also interact with the cytochrome P450 drug-metabolizing system, binding to P450, being oxidized to acetaldehyde by P450, increasing the content of P450, and inducing (causing an increase in the activity of) a unique isozyme of P450. Inhibition of drug oxidation when alcohol is present at the active site of P450 is due to displacement of the drug by alcohol and competition for metabolism; this increases the half-life and circulating concentration of drugs. Induction of P450 by chronic-alcohol treatment

can result in the increased metabolism of drugs, as long as alcohol is not present to compete for oxidation. These pharmacokinetic interactions may contribute to either increased sensitivity or the tolerance observed with alcohol-drug interactions.

Alcohol can affect drug pharmacokinetics by altering drug absorption from the alimentary tract. For example, diazepam (Valium) absorption is enhanced by the effects of alcohol on gastric emptying. Alcohol placed in the stomach at concentrations of 1 percent to 10 percent increases the absorption of pentobarbital, phenobarbital, and theophylline, whereas drugs such as disulfiram and caffeine decrease alcohol absorption by decreasing gastric emptying. Cimetidine (Tagamet)—a drug used to treat stomach ulcers—increases blood alcohol concentrations by inhibiting ADH in the stomach and first-pass metabolism of alcohol. Binding of a drug to plasma proteins will change the effective therapeutic level of the drug, because when the drug is linked to the proteins, it is not available to act on the tissue. Alcohol itself and alcohol-induced liver disease cause a decreased synthesis and release of such plasma proteins as albumin. The resulting hypoproteinemia can result in decreased plasma-protein binding of such drugs as quinidine (Quinidex), dapsone (DDS), triamterene (Dyrenium), and fluorescein (Fluorescite). Alcohol may also directly displace drugs from plasma proteins.

The effects of alcohol on blood flow in the liver are controversial, although most recent reports suggest an increase; this could be significant with respect to metabolism of flow-limited drugs. At higher concentrations, alcohol can act as an organic solvent and "fluidize" cellular membranes, which may increase the uptake or diffusion of drugs into the cell.

METABOLISM

Many alcohol-drug interactions occur at the level of actual metabolism. Ethanol (ethyl alcohol—common in wines and liquors) will compete with such other alcohols as methanol (methyl alcohol—called wood alcohol) or ethylene glycol (antifreeze), for oxidation via alcohol dehydrogenase. In fact, treatment against poisoning by methanol or ethylene glycol involves the administration of ethanol—as the competitive inhibitor—or the addition of inhibitors of alcohol dehydrogenase such as pyrazole or 4-methylpyrazole.

As discussed above, the presence of alcohol will inhibit the oxidation of drugs by cytochrome P450. Alcohol has been shown to inhibit oxidation of such representative drugs as aniline, pentobarbital (Nembutal), benzphetamine (Didrex), benzpyrene, aminopyrine, ethylmorphine, methadone, meprobamate (Equanil, Miltown), phenytoin (Dilantin), propranolol (Inderal), caffeine, tolbutamide (Orinase), warfarin (Coumadin), phenothiazine, benzodiazepine, chlordiazepoxide, amitriptyline (Elavil), chlormethiazole, chlorpromazine (Thorazine), isoniazid (INH), imipramine (Tofranil), dextropropoxyphene, triazolam (Halcion), industrial solvents, and acetaminophen (Tylenol). As this partial list indicates, oxidation of many classes of drugs can be inhibited in the presence of alcohol; these include hypnotics, opioids, psychotropic drugs, anticonvulsants, vasodilators, antidiabetics, anticoagulants, analgesics, and antibacterials. Chronic consumption of alcohol induces the P450 drug-metabolizing system, which could increase oxidation of drugs in sober or abstinent alcoholics. Among the drugs that may be more rapidly metabolized in abstinent alcoholics are ethoxycoumarin, ethylmorphine, aminopyrine, antipyrine, pentobarbital, meprobamate, methadone, theophylline (Bronkodyl, Theo-Dur), tolbutamide, propranolol, rifamycin, warfarin, acetaminophen, phenytoin, deoxycline, and ethanol itself. An important consequence of this ability of chronic ethanol intake to increase drug-clearance rates is that the effective therapeutic level of a drug will be different in an abstaining alcoholic than it is in a nondrinker. This metabolic drug tolerance can persist for several days to weeks after alcohol withdrawal.

PHARMACODYNAMIC IMPLICATIONS

These alcohol-drug pharmacokinetic interactions can have major pharmacodynamic implications. Some examples include the following: The concurrent administration of alcohol plus amitriptyline (Elavil) to healthy volunteers resulted in an increase in the plasma-free concentration of amitriptyline, since the alcohol inhibited drug clearance. Other pharmacodynamic interactions between alcohol and amitriptyline include decreased driving skills (and other psychomotor skills), greater than additive loss of righting reflex, unexpected blackouts, and even death. Laisi et al. (1979) showed that

plasma levels of the tranquilizer diazepam (Valium—an antianxiety drug) were increased in the presence of beer and wine, so the combination of alcohol plus diazepam produced impaired tracking skills, increased nystagmus (nodding off), and impaired oculomotor (eye) coordination, as compared to diazepam alone. Therapeutic doses of the tranquilizers diazepam or chlordiazepoxide (Librium) plus alcohol have been consistently shown to produce impairment of many mental and psychomotor skills; EEG (electroencephalogram) abnormalities could still be detected sixteen hours after administration of fluorazepam in the presence of alcohol to volunteers. Alcohol also decreases the rates of elimination of several benzodiazepines in humans. Phenothiazines and alcohol compete for metabolism by P450, resulting in the decreased clearance of chlorpromazine (Thorazine), for example, and enhanced sedative effects, impaired coordination, and a severe potentially fatal respiratory depression. Alcohol inhibits the metabolism of barbiturates, prolonging the time and increasing the concentration of these drugs in the bloodstream, so that central nervous system interactions are intensified. In humans, alcohol doubles the half-life of pentobarbital; this is associated with a 10 to 50 percent lower concentration of barbiturate sufficient to cause death by respiratory depression, as compared to the lethal dose in the absence of alcohol. Striking pharmacokinetic and pharmacodynamic interactions occur between alcohol and the hypnotic drug chloral hydrate—the so-called Mickey Finn or knockout drops. Alcohol inhibition of morphine metabolism increases morphine accumulation, potentiates central nervous system actions, and increases the probability of death.

OTHER CONSEQUENCES

Pharmacokinetic interactions between alcohol and drugs also have important toxicological and carcinogenic consequences. The metabolism of certain drugs produces reactive metabolites; these are much more toxic than the parent compound. The induction of P450, especially the P4502E1 isozyme by alcohol, results in the increased activation of drugs and solvents to toxic reactive intermediates—such as carbon tetrachloride, acetaminophen, benzene, halothane, enflurane, cocaine, and isoniazid. In a similar manner, procarcinogens—such as aflatoxins, nitrosamines, and aniline dyes—are activated to carcinogenic metabolites after alcohol induction of P4502E1. Since P4202E1 is localized largely in the perivenous zone of the liver cell, the increased activation of these toxins (and alcohol itself) after induction by alcohol may explain the preferential perivenous toxicity of several hepatotoxins, carcinogens, and alcohol itself.

See also **Drug Interaction and the Brain; Drug Metabolism; Psychomotor Effects of Alcohol and Drugs.**

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DRUG INTERDICTION. The *interdiction* of illicit drugs into the United States is the effort to seize them, together with the transport and/or persons that carry them on their way from the producing country to the importing country; many of the seizures occur just as the drugs are brought across the border. The principal drugs subject to U.S. interdiction are cocaine, marijuana, methamphetamine, precursor chemicals for synthetic drugs, and bogus prescription drugs. Unlike other modern nations, the United States has made interdiction, at least for cocaine and marijuana, a significant part of its effort to control the supply of drugs, since about 1975. Both U.S. federal agencies and the military have been involved in this effort. Though interdictors have seized large quantities of drugs, as of 2008 there remained numerous questions about the effectiveness of the program as a method of reducing the use of drugs, particularly cocaine.

Seizures by law enforcement officers are intended to make drug smuggling more risky and less profitable. AP IMAGES

TWO GOALS OF INTERDICTION

Interdiction has two general goals. First, it seeks to reduce the consumption of specific drugs within the nation by making it more expensive and risky for smugglers to conduct their business. Drug seizures raise costs by increasing the amount that has to be shipped in order to ensure that a given quantity will reach the market. An effective interdiction program seeks to raise the probability that a courier is arrested, thereby increasing the price smugglers have to pay to those who undertake the task. These higher fees raise smugglers' costs of doing business and thus the price they must charge their customers, the importers. The combined effect produces increased costs that lead to a higher retail price and serve to lower drug consumption.

At one time it was thought that interdiction could impose a physical limit on the quantity of drugs available in the United States. With a fixed supply available in the producing nations, each kilogram seized on its way to the United States would be one less kilogram available for consumption inside the country. However, this has not proven to be the case. In the early 2000s, it was generally believed that production is expandable and that increased seizures can be compensated for with increases in production, although farmers may have to receive higher prices to provide greater production.

The second, more modest, general goal is to increase the difficulty of smuggling itself and to provide suitable punishment. Smugglers, or at least the principals in smuggling organizations, are among the most highly rewarded participants in the illegal drug trade. Programs are promoted that make their lives more difficult and that subject these criminals to the risks of punishment.

TYPES OF ILLEGAL IMPORTED DRUGS

Three illegal drugs have traditionally dominated imports: heroin, cocaine, and marijuana. Heroin is subject to only modest interdiction efforts because it is usually smuggled in conventional commercial cargo, or it is carried on (or within) the person of the smugglers who travel by commercial traffic (in one method of smuggling heroin, couriers swallow heroin-filled latex balloons before boarding commercial airlines). Seizures are made only in the course of routine inspection of cargo and traffic. It is estimated that ten tons of heroin are smuggled into the United States each year, and seizures of more than ten kilograms are rare. The Drug Enforcement Administration (DEA) annual seizure reports reveal that heroin has a fairly stable market. A total of 805 kilograms of heroin were seized in 2006, about the same amount seized in 1995. Cocaine and marijuana have been the primary targets of interdiction; however, an effective program of interdiction against Colombian maritime

smuggling led to a sharp rise in the share of the U.S. marijuana market served by domestic producers.

The rise in popularity of methamphetamine (meth) has led federal and state governments to impose restrictions on the sale of precursor chemicals needed to make meth. The federal Combat Meth Act of 2006 and laws enacted by over forty states have placed restrictions on the sale of products containing ephedrine and pseudoephedrine—ingredients essential to the production of methamphetamine. These restrictions contributed to a 29 percent reduction in domestic methamphetamine lab seizures in 2005. However, domestic restrictions have fueled the rise in smuggling methamphetamine and precursor chemicals into the United States. As of 2008, domestic production was in the hands of organizations headquartered in other countries with Mexico being a major source of methamphetamine. The United States has worked with Canada and Mexico to limit the amount of legal methamphetamine precursors coming into those countries, and it succeeded in having the United Nations pass a resolution in 2006 that requests governments to work harder against the diversion of chemicals for illicit manufacture. Regarding law enforcement, the United States monitors the shipment of precursor chemicals from Asia to North America and Central America.

The growth of the Internet has also spawned illicit online pharmacies that traffic in legitimate and bogus prescription drugs. Active drug cases involving the Internet rose 25 percent in 2006 over the previous year. The DEA, Federal Bureau of Investigation (FBI), and Immigration and Customs Enforcement (ICE) have increased investigations and asset seizures involving online sale of pharmaceuticals without a prescription. Between 2004 and 2006 the DEA seized more than $52 million in cash, property, and assets from online traffickers. The Food and Drug Administration (FDA) also investigates illicit online pharmacies.

TECHNIQUES

The techniques of interdiction inevitably mirror those of smugglers. Drugs enter the United States by air, land, and sea, by private vessel and commercial carrier. Interdiction must, if it is to have any substantial effect on the drug trade, act against all the modes of smuggling; otherwise smugglers will rely on the mode that is not subject to interdiction.

Interdiction has three separate elements: monitoring, detection and sorting, and pursuit and apprehension. For example, U.S. Coast Guard ships supported by an extensive radar system patrol the Caribbean, which constitutes the major thoroughfare for smuggling from Latin America. The Coast Guard patrol vessels attempt to see, either directly or through radar, all ships moving along certain routes, which constitutes the monitoring activity. The interdictors must then sort, from all that traffic, the relatively small number that are carrying illegal drugs. Finally, they must pursue the smugglers that have been detected, arrest the personnel, and seize the drugs and the ship itself. The interdiction system is as weak as its weakest component; for example, a system that has good pursuit capacities but is unable to sort smugglers from innocents effectively will waste much of that pursuit capacity in chasing nonsmugglers. Similarly, good detection will lead to few captures without effective monitoring capabilities.

The Coast Guard and the U.S. Customs and Border Protection, both part of the Department of Homeland Security (created in the aftermath of the terrorist attacks of September 11, 2001), share primary responsibility for marine and air interdiction. The Coast Guard patrols more distant routes, with U.S. Customs having a greater role in the U.S. coastal zone. Both agencies also conduct interdiction against private planes, with U.S. Customs having primary responsibility over the Mexican land border, a major trafficking area. The DEA has expanded its air surveillance and as of 2007 had a fleet of over one hundred aircraft. The Border Patrol, also a unit of the U.S. Customs and Border Protection, has primary responsibility for the interdiction of drugs carried in cars or on persons crossing the land border. In the late 1990s, new technology, such as x-ray machines that examine commercial vehicles, was installed at border stations in the Southwest. By 2007 more sophisticated electronic surveillance technology was employed along the southwest border. This effort targeted smuggling of both contraband and people.

Both U.S. Customs and the Border Patrol make many seizures and arrests in the course of routine inspection. For example, Customs may find a shipment of cocaine concealed inside a cargo

container being unloaded in the Miami port; the Border Patrol, in the course of pursing illegal immigrants, might find a "mule" (a person) carrying a backpack full of cocaine or heroin. Drugs are shipped in an array of forms; for example, suspended in frozen fruit pulp being imported from Ecuador or in hollowed lumber from Brazil.

MILITARY INVOLVEMENT

For a variety of reasons, there was pressure throughout the 1980s to increase the extent of military involvement in drug interdiction. The drug problem was viewed as a national crisis with an important international element. The military was seen as having unique capabilities, both in its equipment and its training of personnel, to protect the borders.

Historically, the military was ambivalent about engaging in drug interdiction because it viewed this activity as a potential corruption of, and an inappropriate diversion from, its primary mission. With the collapse of its principal strategic enemy, the Soviet Union, the U.S. military became more willing to play a major interdiction role, which was reflected in large increases to the military budgets to handle these new responsibilities. Law in the early 2000s prohibits military personnel from making arrests. Accordingly, military participation has been confined to detection and monitoring rather than pursuit and apprehension. Despite the terrorist attacks of September 11, 2001, and the subsequent wars in Afghanistan and Iraq, military involvement in drug interdiction has continued.

The U.S. Navy provides a number of ships for interdiction patrols in both the Caribbean and the Pacific, combining training with a useful mission. The military runs the integrated radar and communication system that links U.S. Customs, the Coast Guard, the Border Patrol, and other agencies. As of 2008, no significant problems of corruption associated with the military role in drug interdiction had been reported, but relations between the military and the civilian law-enforcement agencies with primary jurisdiction have sometimes been strained, the result largely of differences in organizational cultures.

With the proliferation of U.S. government units involved in interdiction, the need arose for coordinated command. The government has two Joint Inter-Agency Task Forces, one based in Key West, Florida, the other in Alameda, California. These task forces coordinate transit zone activities, including the U.S.-Mexico land border and air and maritime traffic along the borders and sea coasts. The U.S. Interdiction coordinator is the commandant of the U.S. Coast Guard.

EVALUATION TECHNIQUES

Evaluation of the effectiveness of interdiction has been a vexed issue ever since the activity became prominent in the late 1970s. Very large quantities of drugs, particularly of cocaine, have been seized, but the size of such seizures has been cited both as evidence of success and of failure. Some wonder if more cocaine is being seized because interdictors are getting better at their job or because more cocaine is being shipped.

Measuring seizures as a fraction of total shipments (consumption plus seizures) would be helpful, but, unfortunately, consumption is difficult to estimate. Even expressed as a fraction of shipments, seizures are clearly an inadequate measure of the effectiveness of interdiction, since the program imposes two other costs on smugglers—namely, seizure of assets (e.g., boats, planes, real estate, and financial holdings) and the arrest and imprisonment of smuggling agents (e.g., crew members on ships, pilots, and couriers for financial transactions).

Reuter and colleagues (1988) suggest that the most appropriate measure is a price increase in the smuggling sector of drug distribution. Effective interdiction should cause increased smugglers' costs; the increase ought to appear in the difference between the price at which smugglers purchase drugs in the producer country (export price) and the sale price in the importing country (import price). However, the process cannot serve as an operational criterion for any individual component of interdiction, since prices are set in a national market served by all modes and routes of smuggling. Anderberg (1992) concluded that the available data supported only inappropriate and/or inadequate measures of effectiveness, and a more cogent measure requires data that are not available and are not likely to be readily obtained.

One negative consequence of interdiction identified by Reuter and colleagues (1988) has received little attention. By seizing drugs on their way from the source country, interdiction may actually increase export demand for those drugs.

As noted earlier, more stringent interdiction has two effects; it raises prices and thus reduces final demand in the United States, but it also increases the amount that must be shipped to meet a given consumption (because of a higher replacement rate). It appears that, based on reasonable assumptions about the cost structure of the cocaine trade, the second effect has proven greater than the first.

EFFECTIVENESS OF INTERDICTION

Interdiction clearly has had some important consequences for the U.S. drug trade. In contrast to the 1970s, little marijuana in the early 2000s was being imported from Colombia, though that nation remains a low-cost producer. Successful interdiction, particularly against marine traffic from Colombia, imposed such high costs on Columbian imports that both Mexican and U.S. producers came to dominate the U.S. market. Interdiction against Mexican-produced drugs is more difficult and thus the import price of Mexican marijuana is less than that of Colombian.

For cocaine there is much less evidence of success, though interdictors have certainly forced changes in modes of smuggling. In the early 1980s much of the cocaine was brought in by private plane directly from Colombia, but in the early 2000s most of it arrived either by transshipment through Mexico or by commercial cargo. However, though interdictors seize a large share of all shipments, they have not managed as of 2008 to prevent a massive decline in the landed price of the drug. Street prices of cocaine and heroin dropped dramatically between the early 1980s and the early 2000s.

The reasons for this limited success are not hard to identify. Smugglers defray the risks of getting caught by carrying across very large quantities, so that the risks per unit smuggled are low. A pilot who charges $250,000 for the risks (imprisonment, suffering injury or death in the course of landing) involved in bringing across a shipment of 250 kilograms is asking for only one dollar per gram, less than 1 percent of the retail price. Even if interdictors make smuggling much more risky, so that the pilot doubles the demand to $500,000, the higher fee still adds only another 1 percent to the retail price.

Moreover, it is difficult to make smuggling very risky when the United States is determined also to maintain the free flow of commerce and traffic. Hundreds of millions of people enter the country each year; cargo imports also amount to hundreds of millions of tons. Only a few hundred tons of cocaine need to be concealed in that mountain of goods and only a few thousand of those who enter need be in the smuggling business to ensure an adequate and modestly priced supply of cocaine.

Interdiction has accounted for a significant portion of federal government expenditures on drug control. Many critics of the interdiction effort have argued that these resources should be put into drug treatment programs and other programs that could reduce the demand for illegal drugs. Nevertheless, the U.S. government has remained committed to interdiction operations.

See also **Border Management; Dogs in Drug Detection; Foreign Policy and Drugs, United States; International Drug Supply Systems; Operation Intercept; U.S. Government: The Organization of U.S. Drug Policy.**

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DRUG LAWS: FINANCIAL ANALYSIS IN ENFORCEMENT.

Using financial investigative techniques to uncover sophisticated forms of crime began decades ago to bring organized crime bosses to justice. They were charged not with bootlegging or extortion, but for reaping financial windfalls from activities that either were not federal offenses at the time or that prosecutors could not prove. Beginning with the federal tax case

against Al Capone in 1931, Department of Treasury investigators dealt with both the lack of federal laws proscribing racketeering activity and the difficulties in catching underworld bosses for their offenses. The approach was creative but simple: Internal Revenue Service (IRS) agents gathered evidence to prove that the racketeers spent more income than they reported on their tax returns. The difference between what they reported and what the government alleged they earned established that the IRS targets received substantial amounts of unreported income. In an underworld without pay stubs and annual wage statements, how did the government know what the racketeers earned? To tax investigators, it was straightforward: Show how much the person spent—or at least the portion of income spent that could be substantiated.

As Prohibition gave way to different forms of industrial racketeering, syndicated gambling, and drug trafficking, federal agents grew more frustrated over their inability to prosecute increasingly sophisticated criminals. Investigators turned more and more to financial analysis as a means of prosecution. They reasoned that what worked against Al Capone and his cohorts would probably work against other high-profile racketeers who were too insulated by their underlings to be implicated in syndicate transactions.

Proving that individuals—whether they were Mafia bosses or Colombian drug importers—received more income than they could substantiate was difficult. Typically, no records pointed directly to one large unreported sum of yearly income. Rather, evidence of unreported income was gathered by tracing documented purchases that left a paper trail of deposit slips, bank statements, advices, credit card receipts, and mortgages. Investigators soon learned that financial analyses frequently turned up large amounts of money in the possession of people who recently had approved plans for a lucrative drug deal or some other illegal transaction.

For investigators struggling to tie drug traffickers to crimes that had only been planned, finding the proceeds of those transactions was welcome evidence. Money connected the investigator's target to drug or other illegal transactions that other evidence showed they had planned or approved. Drug traffickers and other racketeers who never touched drugs did touch, or otherwise control, the money exchanged for the drugs. Hundreds of criminals have been sent to prison because financial analyses tied large sums to the defendants and their alleged criminal transactions.

As organized crime began to wane in national prominence in the 1970s, an amalgam of homegrown and foreign-based drug traffickers soon took its place. Often as smart and insulated as Mafia bosses, drug traffickers were surprised to find themselves equally vulnerable to cases built on financial evidence. Passage of a number of federal drug reform laws (in 1970, 1978, 1984, 1986, and 1988) added the remedy of asset forfeiture to the government's arsenal of weapons. In order to show that their targets had acquired assets with tainted funds that rendered them forfeitable, investigators resorted to the same financial investigative techniques that had helped build criminal tax cases against underworld leaders.

By the mid-1990s virtually all federal enforcement agencies provided some type of basic training in financial investigation, and several—such as the Drug Enforcement Administration (DEA), Federal Bureau of Investigation (FBI), and Internal Revenue Service (IRS)—have highly specialized programs at their academies. DEA and FBI expert investigators and financial analysts support major drug-trafficking cases by providing evidence of unexplained income to prove the drug charges and to tie the money to drug activity for the purpose of forfeiture.

The USA Patriot Act, enacted following the September 11, 2001, terrorist attacks, gave additional tools to law enforcement to combat money laundering and tax evasion. One provision requires anyone involved in a trade or business, except financial institutions, to report currency received for goods or services in excess of $10,000 on a federal tax form. This information is shared with both the IRS and the Financial Crimes Enforcement Network in the Treasury Department. In addition, a Bulk Cash Statute was passed that authorizes law enforcement to investigate and prosecute persons who transport or attempt to transport currency or other monetary instruments of more than $10,000 from within the United States to outside of the United States, or from outside the United States to within the United

States and knowingly conceal it with the intent to evade federal reporting requirements.

See also **International Drug Supply Systems; Money Laundering.**

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DRUG LAWS, PROSECUTION OF.

Drug arrests in the United States involve a wide variety of controlled substances, including marijuana, cocaine, heroin, methamphetamine, phencyclidine (PCP), prescription medications, and others. An individual may be charged with a number of different offenses, including possession, dealing (selling), and conspiracy to sell. After arrest, the prosecutor exercises broad discretion, choosing from this range of offenses in deciding whether to bring a charge and for what activity. In 2005 the Uniform Crime Reports of the Federal Bureau of Investigation (FBI) estimated that there were about 1,846,400 state and local arrests for drug abuse violations in the United States. Four out of five of these arrests were for possession. In 1987 some 7.5 percent of arrests were for drugs; by 2005 drug arrests accounted for 13 percent of all arrests in the United States.

Drug offenses can violate either federal or state laws. Since the majority of arrests are made by local law-enforcement officials, most defendants are charged in state courts. The cases received by federal prosecutors, called U.S. attorneys, from such federal enforcement agencies as the FBI or the Drug Enforcement Administration (DEA), frequently involve more complex matters such as drug trafficking. However, the volume of federal drug prosecutions rose in the 1990s, as tougher federal drug laws and sentencing provisions led state prosecutors to refer these cases to federal jurisdiction. In addition, federal prosecutors have used the Racketeer Influenced and Corrupt Organizations Act (RICO) to prosecute drug traffickers and to confiscate property used in drug enterprises. The federalization of drug crimes has had a profound impact on the work of the federal courts and the budget of the federal prison system.

In determining what charges should be filed against the offender, the prosecutor examines many factors: the criminal history of the defendant, the seriousness of the drug involved, and the quality of the evidence. Most states give the prosecutor the discretion to charge an enhanced-penalty crime for a repeat offender.

The vast majority of the cases lead to guilty pleas, through some form of plea bargaining between the prosecutor and the defense attorney. In these agreements, which must be approved by the court, the defendant pleads guilty, often in return for a fine, court-ordered counseling, or a lessened prison term. Repeat offenders face tougher agreements.

In deciding what plea to accept, prosecutors consider many of the same factors they did when they brought the original charges. A critical factor is the quality of the evidence. Many drug cases are easy to prove because the defendant purchased or sold the drugs directly to a police officer or because a search warrant leads to the discovery of drugs in an area controlled by the defendant. Prosecutors face much more difficult challenges in convicting suspects involved in complicated conspiracy charges such as those associated with the shipment or distribution of drugs. In many drug prosecutions, motions to suppress evidence are filed by defense attorneys to determine whether the search that turned up the drugs violated the Search and Seizure Clause of the Fourth Amendment. During the 1990s and into the first decade of the twenty-first century, a more conservative U.S. Supreme Court has made it much more difficult to suppress drug evidence, whether seized with or without a search warrant.

Another important factor involves the level of cooperation provided by the defendant. The prosecutor often accepts a more lenient agreement for defendants who assist law-enforcement officers and/or testify in court concerning who sold them

the drugs they possessed or resold. These plea agreements allow the police to target other offenders and also relieve the pressure on the courts. Plea bargaining does, however, raise serious questions in the public's mind about the dangers of leniency; it raises other questions, among defendants and their attorneys, about equity and fairness. Additionally, narcotics officers and prosecutors often disagree about the outcome or the handling of a case. These differences are often mediated by task forces in which prosecutors with specialized drug experience are assigned to work with a select group of narcotics officers.

Generally less than 10 percent of drug cases go to trial. In a trial the police officer is a witness in the case brought by the prosecutor. By questioning the officer, the prosecutor—as lawyer for the state—elicits evidence designed to show that the defendant possessed or sold drugs.

Ultimately, the judge determines the actual sentence. Beginning in the late 1980s, federal and state sentencing guidelines limited judicial discretion, requiring judges to impose sentences based on the severity of the criminal offense and the criminal history of the defendant. However, in 2005 the Supreme Court struck down the federal sentencing guidelines, ruling them a violation of the Sixth Amendment. Though the guidelines were subsequently viewed only as advisory, in a 2007 case the Supreme Court made clear that the guidelines must be consulted by the federal courts to determine whether a sentence is deemed reasonable. Many criminal statutes avoid the guidelines entirely by imposing mandatory minimum sentences for drug crimes. But commonly in a plea agreement or after trial, the prosecutor can modify the severity of the sentence by reducing the charge or by recommending that the court reduce the sentence. Across the United States, and even within large counties, great differences occur in sentencing and in sanction recommendations.

DRUG COURTS AND FORFEITURE LAWS

Participants in the criminal justice system recognized that drug-related crimes should be addressed in different ways. The emergence of drug courts in the 1990s signaled a new way of prosecuting drug offenders. Drug courts seek to reduce drug use and associated criminal behavior by retaining drug-involved offenders in treatment. Drug courts divert drug offenders from jail or prison by referring them to community treatment. Defendants who complete the program either have their charges dismissed or probation sentences reduced. A 1994 federal law authorized the U.S. attorney general to make grants to state and local governments to establish drug courts. These grants proved effective. By 1999, some 416 drug courts were operating in the United States, with over 270 more in the planning stages. By 2007 the numbers had jumped dramatically: 1,699 drug courts were in operation, with another 349 in the planning stage. These courts shift discretion from the prosecutor and place it with the judge, who has broad discretion in a drug court.

Federal and state prosecutors have also used asset forfeiture laws to attack drug traffickers. Forfeiture laws authorize prosecutors to file civil lawsuits asking a court for permission to take property from a criminal defendant that was either used in the crime or was the fruit of a criminal act. In 2005 over $1.25 billion in assets was seized by federal agencies.

Aside from civil forfeiture, prosecutors have also used tax and money laundering laws to prosecute drug traffickers. The USA Patriot Act, enacted following the September 11, 2001, terrorist attacks, sought in part to combat money laundering and tax evasion. One provision requires anyone involved in a trade or business, except financial institutions, to report currency received for goods or services in excess of $10,000 on a federal tax form (financial institutions have reported similar cash transactions to federal authorities since the 1990s.) Another provision, the Bulk Cash Statute, authorizes law enforcement to investigate and prosecute persons who transport or attempt to transport currency or other monetary instruments of more than $10,000 outside the United States or who bring large amounts of currency into the United States.

Prosecutors sometimes employ non-criminal statutes and ordinances to attack drug crimes. For example, prosecutors may use public nuisance laws, zoning laws, and public health laws to remove drug offenders from property where drugs are being used and sold. Though the legal action is addressed to the landlord or property owner, it has the effect of removing drug users and traffickers from

apartments and houses. Increasingly, cities are condemning and destroying buildings that have been used as crack houses and meth labs.

See also **Exclusionary Rule; Mandatory Sentencing; Rockefeller Drug Laws.**

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DRUG METABOLISM. Most drugs are taken by mouth and, in order to be absorbed through the stomach and intestine, they need to be lipid-soluble. This solubility permits them to easily cross the membrane barrier. After absorption, organs with plentiful blood-flow such as the brain, liver, lungs, and kidneys are first exposed to the drug. Only highly lipid-soluble drugs can enter the brain by crossing the blood-brain barrier.

Drug concentration at the target organ is an important index for therapy and generally has an optimal range. The drug level can be raised by increasing dose, or by more frequent administration, but too high a level could cause toxicity. The drug level at the target organ can also be lowered by elimination through the urine or by metabolic steps that convert the drug to more water-soluble forms. Water-soluble metabolites are eliminated quickly in the urine. Most drugs given orally are lipid-soluble enough to be reabsorbed in the kidneys and are eliminated only slowly in small amounts in the unchanged form in urine. Therefore drug metabolism is an important factor that controls drug levels in the body, because without the metabolic step the drug usually remains in the body or accumulates if it continues to be taken. Drug metabolism is a biochemical process and involves enzymes; drugs are metabolized sequentially or by parallel pathways to various products called metabolites. Many enzymes have been identified and some are very specific for drugs or substrates, whereas others have broad or less stringent structure requirements.

Many factors can modify drug metabolism. Genetic factors or inherited deficiency of an enzyme could cause accumulation of certain drugs. Increased levels and increased toxicity may be caused by inhibition of drug metabolism by other concurrently administered drugs. Decreased plasma levels of drugs after repeated administration have been observed and this is attributed to increased enzyme activity by a process called induction; auto-induction causes the increased metabolism of the inducing drug and cross-induction refers to the accelerated metabolism of other drugs.

DRUG-METABOLIZING ENZYMES

Drug-metabolizing enzymes change the chemical nature of drugs by inserting oxygen, hydrogen, water, or small molecules such as amino acids and sugar molecules. The resulting metabolites may thus contain hydroxyl (the univalent group or ion OH), or hydrogenated or hydrolysis products, or be conjugated with sugar or other functional groups. By far the most commonly occurring metabolic step is hydroxylation (the addition of oxygen) by the enzyme oxygenase—and this will be discussed in detail.

OXIDATION BY CYTOCHROME P450 MONOOXYGENASE

Oxygen is vital for living organisms, and enzymatic reactions involving this molecule for drug metabolism are numerous and well characterized. Lipid-solubility is an important factor for absorption across the stomach and intestinal wall, and the insertion of an oxygen atom to lipid-soluble compounds results in hydroxylated groups (−OH) that

are more water-soluble than the parent compound. The pioneering work on the oxygenation reaction involved the metabolism of barbiturates, a class of centrally acting drugs very popular in the 1950s. A long-acting barbiturate, phenobarbital, very slowly hydroxylates compared to other barbiturates, such as hexobarbital, pentobarbital, and secobarbital. The oxygenation enzymes involved were named cytochrome P450 after the wavelength of light they absorbed in a spectrophotometer (peak at 450 nanometers [nm]). Subcellular fractionation by centrifugation yielded "microsome" pellets which contained the cytochrome P450 activity. Cytochrome P450 is most abundant in the liver and, before the full nature of cytochrome P450 was known, the microsomal oxygenase was often called mixed function oxidase. Cytochrome P450 consists of a superfamily of enzymes, with wide and sometimes overlapping substrate specificities.

Although phenobarbital is no longer widely used for therapeutic purposes, because of better alternatives with fewer side effects, it is an excellent inducer of certain forms of cytochrome P450 (e.g., the CYP2B family).

Other important drugs of abuse that are metabolized by cytochrome P450 include benzodiazepines (tranquilizers such as diazepam [Valium], chlordiazepoxide, alprazolam, triazolam) and opioids (codeine, oxycodone, dextromethorphan). The first group of drugs is hydroxylated and the second group is metabolized by loss of a carbon moiety (dealkylation). The dealkylation reactions are also mediated by cytochrome P450.

Many cytochrome P450 enzymes have been isolated and characterized. With molecular biology techniques, the genetic code DNA has been identified for many cytochrome P450 enzymes. Among these, two forms of cytochrome P450 are known to be deficient in certain individuals. In the mid-1970s, a deficiency of the specific cytochrome P450 called CYP2D6 was independently reported for sparteine (a labor-inducing or antiarrhythmic drug) and for debrisoquine (an antihypertensive agent). Since then, more than thirty clinically useful drugs have been shown to be metabolized by this enzyme. The presence of this cytochrome P450 in a population is polymorphic, that is, some people lack this enzyme. A simple urine test using dextromethorphan, a cough suppressant, is commonly used to identify the enzyme deficiency in a patient. Another cytochrome P450 deficiency involves metabolism of mephenytoin (CYP2C type) but not many drugs are metabolized by this enzyme. The frequency of both deficiencies were first established in Caucasians, and CYP2D6 deficiency was reported to be 7 percent while CYP2C deficiency was 3 percent. Because of the presence of deficient subjects, the population data do not show a bell-shaped normal distribution curve but rather a bimodal distribution indicating polymorphism.

ALCOHOL METABOLISM

Alcohol (ethanol) metabolism predominantly involves a type of oxidation called dehydrogenation (loss of hydrogen) and the subcellular fraction called the mitochondria is the major site. Alcohol is metabolized by successive dehydrogenation steps, first producing acetaldehyde and secondly acetic acid. The major organ for alcohol metabolism is the liver. In heavy drinkers, however, alcohol induces another enzyme, cytochrome P450, and the proportion of the metabolism by this route compared to dehydrogenation becomes significant. Because the amount of alcohol ingested must be relatively large to have pharmacological effects, the amount of alcohol exceeds the amount of enzyme, resulting in saturation. Acetaldehyde, in general, is toxic because it is reactive and forms a covalent bond with proteins. When the enzyme that metabolizes acetaldehyde to acetic acid is inhibited by an external agent, acetalaldehyde levels increase and produce a toxic syndrome. Inhibitions of this enzyme, such as disulfiram (Antabuse), have been used in the treatment of excessive drinking.

TRANSFERASES FOR CONJUGATION/ SYNTHETIC REACTIONS

Products formed by oxidation (e.g., by cytochrome P450) are often metabolized further with small molecules such as glucuronic acid (glucose metabolite) or sulphate. The enzymes involved are called transferases. Other conjugation reactions are carried out by transferases linking glutathione with reactive metabolic products, acetyl-CoA with an amino group on aromatic rings, and glycine (amino acid) with salicylate.

Glucuronic-acid conjugations are catalyzed by various forms of glucuronyl transferases, which

appear to have broad substrate specificity. Glucuronide conjugates are very water-soluble and likely to be quickly eliminated via the kidneys. The plasma levels of glucuronide conjugates of oxazepam (a benzodiazepine antianxiety agent) are, however, several-fold higher than the parent drug. This can be explained by the relatively rapid process of conjugation reaction in the liver compared to the renal (kidney) clearance of its conjugate. Because glucuronidation involves a glucose metabolite, which is abundant, the transferase would not reach saturation easily, although sulfo-transferase utilizes the sulphate which is of limited supply via foods and can be saturated. For example, acetaminophen (Tylenol) forms both glucuronide and sulfate conjugates and the sulfation process can be easily saturated after a few tablets.

Glutathione conjugation is very important as a detoxification pathway. Unstable or reactive metabolites formed from other metabolic reactions may cause toxicity by reacting with so-called house-keeping enzymes in the body. Glutathione, because of its abundance, can react with these metabolites instead and acts as a scavenger; an epoxide whose formation is catalyzed by cytochrome P450 is detoxified, except in an overdose case, by glutathione transferase. Some epoxide intermediary metabolites have been shown to be ultimate carcinogens, and detoxification by gluthione would be beneficial.

Glycine is the smallest amino acid and the conjugation with salicylic acid (formed rapidly from aspirin) is the major metabolic pathway for salicylates. Salicylate poisoning, especially in children, was very common before the introduction of the child-proof cap for drug containers in the 1960s. The difficulty of treating the salicylate poisoning was due to saturable glycine conjugation; the higher the dose, the slower was the rate of elimination.

Acetylation is also important for the detoxification of carcinogens containing aromatic amines. One form of N-acetyltransferase is polymorphic (people have different forms of the enzyme). The frequency of slow acetylator types shows a large variation ranging from 5 to 10 percent in Oriental and Inuit (Eskimo) subjects to as high as 50 percent in Caucasians and Africans. Drugs affected by this genetic polymorphism are isoniazid (antituberculosis), procainamide (antiarrhythmic), sulfamethazole (antibiotic), and other amine-containing compounds.

CLINICAL CONSEQUENCES

Drug metabolites are often pharmacologically less active than the parent drug. Yet some biotransformation products are active—for example codeine is relatively inactive but is metabolized to the active drug morphine. Because the liver is the major site of drug metabolism, acute or chronic liver diseases would alter drug metabolism, resulting in prolonged drug half-lives and effects.

See also **Complications: Liver (Metabolic); Drug Interaction and the Brain; Drug Interactions and Alcohol.**

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DRUG POLICY ALLIANCE (DPA).

The Drug Policy Alliance (DPA) is a not-for-profit organization established to advance those policies and attitudes that best reduce the harms of both drug misuse and drug prohibition and to promote the sovereignty of individuals over their minds and bodies. DPA envisions a just society in which the use and regulation of drugs are grounded in science, compassion, health, and human rights; in which people are no longer punished for what they put into their own bodies, but only for crimes committed against others; and in which the fears, prejudices, and punitive prohibitions are no more.

Headquartered in New York, DPA has eight offices, 50 staff, 25,000 dues-paying members, more than 50,000 online subscribers, and a growing

track record of success at the local, state, and federal levels. DPA's New York-based Lindesmith Library contains more than 10,000 books, reports, government documents, periodicals, videos, and articles on drugs and drug policy; and its $1.5 million Advocacy Grants Program funds allied organizations and efforts.

BRIEF HISTORY

The Drug Policy Alliance was formed in July 2000 when the Lindesmith Center, an activist drug policy think tank established in 1994, merged with the Drug Policy Foundation, a membership and grant-making organization established in 1987, to create an umbrella organization working for drug policy reform. The Lindesmith Center (TLC) was founded in 1994 by Ethan Nadelmann, JD, PhD, a professor of politics at Princeton University, whose writings on drug policy had attracted international attention. The Lindesmith Center, named after Professor Alfred Lindesmith—an Indiana University professor who was the first prominent scholar in the United States to challenge conventional thinking about drugs, addiction, and drug policy—became the first domestic project of George Soros's Open Society Institute (OSI), an operating and grant-making foundation established in 1993 that promotes democratic institutions in Central and Eastern Europe and the former Soviet Union.

The Drug Policy Foundation (DPF) was founded in 1987 by Arnold S. Trebach, JD, PhD, a professor at American University, and Kevin B. Zeese, an attorney who had directed the National Organization for Reform of Marijuana Laws (NORML) in the early 1980s. They envisioned DPF as "the loyal opposition to the war on drugs" and introduced a number of initiatives that have defined the drug policy reform movement ever since. These included an annual drug policy reform conference (which shifted to a biennial conference in 2001), a regular publication series, and an awards program to recognize achievement in various fields of drug policy reform. DPF was also the first and most significant effort to build a membership organization around drug policy reform.

On July 1, 2000, these two organizations merged to create the Drug Policy Alliance with the objective of becoming a powerful advocacy organization nationally and internationally. DPA has worked in tandem with various 501(c)(4) affiliates, including the Drug Policy Alliance Network, the Center for Policy Reform, the Campaign for New Drug Policies, and Americans for Medical Rights.

DRUG POLICY REFORM MILESTONES

- The Lindesmith Center collaborated in 1995 with the OSI program on public health to create the International Harm Reduction and Development program, which has since advanced harm reduction in Central and Eastern Europe, the former Soviet Union, and Asia.
- DPA affiliates were primarily responsible in California (1996), Alaska (1998), Oregon (1998), Washington (1998), Maine (1999), Colorado (2000), Nevada (1998 and 2000), and New Mexico (2007) for making cannabis legally available to seriously ill patients and reducing criminal penalties for possession, objectives supported by roughly three out of four Americans.
- The Lindesmith Center published in 1997 *Marijuana Myths, Marijuana Facts: A Review of the Scientific Evidence*, by Lynn Zimmer, PhD and John P. Morgan, MD. Fifty-thousand copies have been sold and it is available in seven languages.
- The Safety First Project was launched in 1998 to provide parents, teens, and educators with information about marijuana and other drugs, as well as realistic options for dealing with drug use by promoting reality-based models based on comprehensive sex education. It has worked closely and affiliated with the California Parent-Teacher Association. DPA has distributed worldwide more than 225,000 copies (in nine languages) of *Safety First: A Reality-Based Approach to Teens, Drugs, and Drug Education* (2007) by Dr. Marsha Rosenbaum, who founded the Safety First program. DPA also publishes *Beyond Zero Tolerance: A Reality-Based Approach to Drug Education and School Discipline* (2007) by Dr. Rodney Skager and *Making Sense of Student Drug Testing: Why Educators Are Saying No* (Kern et al., 2004).
- The Lindesmith Center drafted an open letter to United Nations Secretary General Kofi Annan in anticipation of the 1998 U.N.

General Assembly Special Session on the World Drug Problem. The letter was signed by more than 500 prominent political leaders, scholars, academics, and scientists from around the world and appeared in the *New York Times*.

- In 2000 Ethan Nadelmann and the Lindesmith Center worked closely with Arianna Huffington's Shadow Conventions to host two four-day forums in Los Angeles (alongside the Democratic National Convention) and Philadelphia (alongside the Republican National Convention) to highlight bipartisan neglect of key social issues, including the drug war, income inequality, and campaign finance reform.
- DPA supported California's landmark treatment-not-incarceration law, Proposition 36, approved via ballot initiatives by 61 percent of California voters in November 2000. Proposition 36 allows first- and second-time nonviolent drug offenders the opportunity to receive substance abuse treatment instead of jail time. More than 84,000 people were diverted from jail or prison to drug treatment and graduated from the program in the first five years after Proposition 36 became law, saving taxpayers at least $1.5 billion.
- In 2005 DPA New Mexico assembled stakeholders from around the state to form the New Mexico Methamphetamine Working Group, co-chaired by the governor's drug czar and the director of DPA New Mexico. The working group produced the first statewide "four pillars" approach to methamphetamine in the United States that emphasizes the principles of harm reduction. DPA New Mexico subsequently received a $500,000 grant from the U.S. Justice Department to create a statewide methamphetamine education and prevention program.
- DPA New Jersey supported the "Bloodborne Pathogen Harm Reduction Act," which was signed into law in 2006. The law allows up to six cities to establish syringe access programs to help prevent the spread of HIV/AIDS, hepatitis C, and other blood-borne diseases. Previously, DPA played a pivotal role in successful efforts to make syringes legally available in New York (2000) and California (2004) and supported successful efforts in Connecticut, Illinois, and other states.
- DPA has worked across the country to pass 911 Good Samaritan immunity laws. The first of these was enacted in New Mexico, where DPA wrote and led the successful campaign in 2007 to eliminate fear when calling 911 for help during an overdose. The law provides limited immunity from drug possession charges when a drug-related overdose victim or a witness to an overdose seeks medical assistance.
- DPA has built broad coalitions to eliminate mandatory minimum sentencing (in Alabama, New York, Maryland, and Wisconsin) and racially biased crack/cocaine sentencing at the state (in Connecticut and California) and federal levels.

See also **Legalization vs. Prohibition of Drugs: Policy Analysis.**

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ETHAN NADELMANN

DRUG TESTING METHODS AND CLINICAL INTERPRETATIONS OF TEST RESULTS. As interest increases in employment-related drug testing, the technologies and the interpretive skills of analysts continue to evolve. Although recent literature indicates that significant refinements and modifications to drug testing technology have been made, the complexity of drug effects is so great that many problems exist in interpretation of the test results. The most frequent problems that confront the toxicology laboratory relate to developing technology that can determine how much and when the drug was taken, how long after use the tests are capable of showing positive results, the causes and rates of false positive and false negatives, and how tests can be "beaten" by employees. These problems will be discussed and the various laboratory procedures that are used to combat these problems will be examined.

DRUG PROPERTIES: ABSORPTION, DISTRIBUTION, AND ELIMINATION PHASES

Detection of a drug depends largely on its absorption, distribution, and elimination properties. There are various routes of drug administration; oral (e.g., drinking alcohol or swallowing pills), intravenous (e.g., heroin injected into a vein) and inhalation (e.g., smoking marijuana; snorting cocaine; sniffing glue). Drugs taken orally are usually the slowest to be absorbed (i.e. the speed at which the drug reaches the brain and other body organs) whereas intravenous and inhalation routes result in the fastest absorption. Once the absorbed drug enters the blood stream it is rapidly distributed to the various tissues in the body. The amount of drug stored depends on the nature of the drug, the quantity, duration of ingestion, the tissue holding the drug and the frequency of use.

Some drugs are fat-soluble and are deposited in fat tissues. For example, δ^9-tetrahydrocannabinol (THC), the active ingredient in marijuana, is highly fat-soluble, resulting in rapid reductions in blood levels as the drug is being distributed to the various tissues. Blood levels of δ^9-THC peak and start to decline in half the time it takes to smoke a marijuana "joint." Concentrations are known to fall by almost 90 per cent in the first hour. Depending on the amount of drug stored in the fat tissues, detection may be possible in the urine for many days after last use. There are cases where marijuana metabolites have been detected for as long as sixty days after last use, since small amounts from fat go back into blood and appear in the urine. Ethanol or ethyl alcohol (the beverage alcohol) is not fat-soluble but is distributed in the total body water. Since blood is mostly made up of water, the presence of alcohol is easier to detect than fat-soluble drugs like δ^9- THC.

The "absorption" and "distribution" phases are followed by an "elimination" phase. The liver is the major detoxification center in the body where the drugs are metabolized as blood circulates through this organ. The metabolites are then excreted into the urine through the kidneys. At the same time, drugs deposited in fat tissues are also slowly released into the blood stream and metabolized.

Drugs vary by their elimination half-life. An elimination half-life is the amount of time needed for the drug level to fall by 50 percent. Every half-life the drug level falls by 50 percent. Table 1 shows the impact of the half-life on the amount of drug left in the body. At the end of seven half-lives over 99 percent of the drug will be eliminated from the body. (See Table 2 for drug half-lives). The half-life of a drug is heavily influenced by a variety of factors including the individual's age, sex, physical condition as well as clinical status. A compromised liver and concurrent presence of another disease or drug have the potential of enhancing the toxic effects of the drug by slowing down the elimination process. Under different clinical conditions, however, this process may be speeded up. Therefore, great variation can be found in the half-lives of the same drug.

Approximately seven half-lives are required to eliminate 99 per cent of any drug. Because cocaine's half-life is relatively short, averaging one hour, only six hours are needed for elimination of 99 per cent of the drug. On the other hand, cocaine's metabolites have a longer half-life and can be detected for a considerably longer period of time through urine drug assays. Compared to cocaine, phenobarbital has a much longer half-life of 80–120 hours, so that at least 480 hours (or 20 days) are required to eliminate 99 per cent of the drug. Since there is much variation in the half-life of different drugs

	Amount of drug left in the body	Amount of drug eliminated
Start	100%	100%
End of 1st half-life	50.0%	50.0%
End of 2nd half-life	25.0%	75.0%
End of 3rd half-life	12.5%	87.5%
End of 4th half-life	6.25%	93.75%
End of 5th half-life	3.125%	96.87%
End of 6th half-life	1.56%	98.44%
End of 7th half-life	0.78%	99.22%

Table 1. Impact of half-life. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

and the absolute amount of drug present can be very small, it is crucial that the appropriate body fluid for analysis is selected for testing.

Ethanol is absorbed from the stomach by simple diffusion. Gastric absorption is fastest when strong drinks, distilled spirits containing 40 to 50 percent ethanol by volume, are consumed. Dilute beverages, such as beer (4–5% ethanol) or wine (11–12% ethanol) are absorbed slowly. Alcohol is absorbed very rapidly from the small intestines. The essential action of food is to delay gastric emptying and thus slow the absorption process. Typically, studies have shown that peak BAC is reached between 30 minutes and 90 minutes of consumption; earlier on an empty stomach and later on a full stomach. Once absorbed, ethanol rapidly diffuses throughout the aqueous compartments of the body, going wherever water goes.

Absorption, distribution into different tissues, and elimination are dynamic processes and take place simultaneously. The rate of removal of ethanol from the body is the sum of the rates of excretion in urine, breath, and sweat, and the rate of the metabolism in the liver and other tissues. In humans, alcohol metabolism follows a "zero" order kinetics, i.e., it is largely independent of alcohol concentration in the blood and its levels decline almost linearly over time. The implication of this is that BAC falls at a constant rate over time. In social drinkers it is from 0.015 to 0.018 percent (15 mg/100mL to 18 mg/100mL) per hour and in heavy drinkers it is typically between 0.018 and 0.025 percent (18mg/100mL to 25mg/100mL) per hour. In the alcoholic patient, the elimination rate is generally higher. In forensic calculations, a rate of 0.015 percent (15mg/100mL) per hour is usually used. In our studies we have found 0.018 percent (18mg/100mL) per hour to be the average rate of metabolism. The larger the dose of alcohol given, the longer the duration of the measurable blood alcohol concentration.

SELECTION OF DRUGS TO BE TESTED

A number of different criteria can be applied to the drug(s) or category of drugs that should be tested or monitored. Drug availability, clinical effects, and robustness of the analytical method(s) used for analysis are probably the most important.

Availability. Prescription patterns of psychoactive and other drugs vary from place to place and country to country. Abuse of benzodiazepine nitrazepam is common in Europe but almost unknown in North America, since it is not sold here. The psychoactive chemical cathinon (cathine), the active ingredient in the leaves of the khat plant, is chewed in northeast Africa, is not a problem in North America. Codeine, an opioid available in Canada as over-the-counter preparations, is sold only by prescription in the United States.

A wide availability of "legal" stimulants poses an interesting problem since they are a common finding in accident victims. A study carried out by the U.S. National Transportation Safety Board from October 1987 to September 1988 showed that over-the-counter stimulants—such as ephedrine, pseudoephedrine and phenylpropanolamine—were commonly found among drivers killed in heavy truck accidents. Amongst the eight States that participated in this safety study almost all amphetamine use was in the California region. Similar findings are also reported from emergency rooms over the past five years as well as from admissions in a trauma unit due to motor-vehicle accidents. All this suggests that drug use varies not only from place to place but also region to region within a given country.

Thus, the selection of a drug to be tested and monitored, appropriate for one country and place, may not necessarily be appropriate for another country.

Clinical Effects. Drugs that manifest abuse potential and impair behavior such that job performance

can be affected are prime candidates for testing or monitoring in the workplace. Alcohol and cocaine are examples of this.

Analytical Methods. A false positive finding can have a serious impact on the livelihood of the person being tested. Therefore, special attention needs to be paid to the testing methods. Ideally the analytical method should be specific for the drug being tested (i.e., no false positive), easy, and inexpensive to perform. Confirmation methods should also be readily available. Availability of technical and scientific expertise to perform the tests is also essential.

Interpretation of the analytical results also needs to be carefully considered as even a normal diet can result in a positive drug identification. For example, poppy seed ingestion can result in a true positive *analytical* result (opiates, like heroin, are derived from the poppy plant *Papaver soniferum*) but it is a false positive for drug use. Some ethnic diets may also lead to these confounding problems, as when food containing poppy seeds is eaten during Ramadan.

What should be analyzed? Ideally the analysis should look for the parent drug rather than its metabolite, although this may not always be possible as some drugs are very rapidly metabolized (e.g., heroin metabolism to morphine). Sensitivity of the analytical procedure should be dictated by the drugs' psychoactive pharmacological properties. If the drug is shown to be devoid of abuse potential then its detection beyond the time of pharmacological activity, although important in the clinical management of the patient, does not necessarily serve a useful purpose for a workplace drug screening programme.

The guidelines developed by the National Institute on Drug Abuse in April 1988 address five "illegal" drugs: marijuana, phencyclidene, amphetamine, cocaine and heroin. Rapid screening methods that allowed for "mass screening" were available at that time, as were the confirmation methods for these five drugs. Mood altering substances such as benzodiazepines, barbiturates and some stimulants such as antihistamines are at present excluded from these regulations in the United States. This is probably due to the wide availability of these drugs as medications within the general population and the technological requirements for screening and monitoring of these drugs.

TYPES OF TESTING: BLOOD, URINE, AND HAIR SPECIMENS

Blood and urine are the most commonly used biological fluids in the analysis for drugs other than alcohol. Blood, obtained by an invasive procedure, is available only in small quantities and drug concentration levels in blood are typically low. Urine is the preferred sample of choice as it is available in larger volumes, contains the metabolite and requires less invasive procedures in its collection. Both sampling procedures, however, are limited in their ability as they only determine the absolute amount of drug present in the fluid being examined. This quantity is dependent upon the amount of the drug used, when it was last used, as well as the half-life of the drug.

Recently, hair samples have been used to detect drug use. A number of technical problems must be overcome before hair can be used as a definitive proof of drug use. Hair treatment and environmental absorption are but two of the many concerns and problems that have been cited. An advisory committee of the Society of Forensic Toxicology has recently reported that "The committee concluded that, because of these deficiencies, results of hair analysis alone do not constitute sufficient evidence of drug use for application in the workplace."

Various body fluids such as sweat, saliva, blood, urine, and breath, have been used for alcohol analysis. Breath, though not a body fluid, is commonly used by law enforcement authorities. Although a number of variables can affect breath/blood ratio, a 2100:1 alveolar breath/blood conversion ratio has been used and accepted for use with breathalyzers. Breath-testing equipment calibrated with a blood:-breath conversion factor of 2100 consistently underestimate actual blood alcohol concentrations (BAC). Accuracy of breath analysis results is subject to various instruments and biological factors. Potential errors in breath analysis can also be caused by the presence of residual alcohol in the mouth. Immediately after drinking there is enough alcohol vapour in the mouth to give artificially high concentrations on breath analysis. Generally this effect disappears twenty minutes after drinking but high values for as long as forty-five minutes have been reported.

As of the early 1990s, all existing technologies are limited in terms of determining how much or when the drug was consumed.

Blood and saliva concentrations reflect the current blood alcohol concentration, but generally a blood sample is used in hospitals to access the patient in the casualty wards. In programs requiring monitoring of alcohol use, urine is probably the sample of choice. Urine alcohol concentration, which represents the average blood alcohol concentration between voiding, has the potential of being "positive" while the blood may be "negative."

MEASURING IMPAIRMENT

Except for alcohol, the degree to which a person is influenced or impaired by a drug at the time of the test cannot be determined from test results alone. Correlations between positive blood levels and degree of impairment are usually stronger than correlations between urine levels and degree of impairment; however, neither blood nor urine tests are sufficiently accurate to indicate impairment even at high levels of concentration. Human studies using marijuana and cocaine have shown that a "perceived high" is reached *after* the drug concentration has peaked in the blood. Generally, blood can only show positive results for a short time after drug consumption, whereas urine can be positive for a few days to weeks after last use. For example, metabolites of δ^9-THC (active ingredient in marijuana) that are lipid-soluble can be detected in the urine from a few days to many weeks, depending on the drug-habit of the user. Excretion of the drug in urine and its concentrations are also affected by several factors, such as dilution and pH (acidity) of the urine. There have been many cases where a strong, positive urine sample for cannabinoids was found in the morning, a borderline positive in the afternoon, followed by a strong positive the next morning; there have been similar cases with respect to phenobarbital.

A positive urine test cannot reveal the form in which the drug was originally taken—or when and how much was taken. For example, crack-cocaine, impure cocaine powder, or cocaine paste (which can be smoked, inhaled, injected, or chewed) all give the same result in the urine test. The consumption of poppy seeds has been reported to give positive results for opiate use, because some seeds contain traces of opiates and some have been known to be contaminated with opium derivatives. Similarly, consumption of herbal coca tea has resulted in positive results for cocaine use. These diverse incidences illustrate the difficulties involved in measuring impairment using urine results.

The problem of interpreting urine-test results is one of the major bases of concern for restricting their use in the employment setting. Even the effectiveness of preemployment drug-screening tests, due to the difficulties in interpretation is being questioned. Based on a study of 2,229 preemployment drug screening tests and follow-up, one group of researchers have come to the following conclusion: "our findings raise the possibility that a preemployment drug screening may be decreasingly effective in predicting adverse outcomes associated with marijuana use after the first year of employment." They make a similar comment about cocaine.

There is no threshold for alcohol effects on performance or motor-vehicle-accident risk. Although the effects of alcohol on impairment and crash risk appear more dramatically above 80mg/100mL, a review of literature would suggest that impairment may be observed at levels as low as 15mg/100mL. It is not possible to specify a blood alcohol concentration level above which all drivers are dangerous and below which they are safe or at "normal" risk. An author of a major literature review on the behavioral effects of alcohol concluded "that alcohol sensitivity can vary from time to time, person to person, and situation to situation, the setting of a "safe" BAC will always be arbitrary, being based on a low, but a nonzero, incidence of effects below that level" and "the most striking feature to emerge from any review of the effects of alcohol on behavior is the marked lack of agreement between authors, amounting, in many instances, to direct contradiction. This is especially true for the effects of smaller dose."

"Legal" BAC levels differ in different countries. Some even have more than one legal limit over which the driver of a vehicle is considered as "impaired." Some European countries have 50mg/100ml; others have 80mg/100ml as their legal limits. In the United States, the legal limits vary from 80mg/100mL to 100mg/100mL in different states, but employees who are regulated by the U. S. Department of Transportation have a BAC legal limit of

Drug	Half-life (t2)	Detection period
Methamphetamine	12–34 hours	2–3 days
Amphetamine (metabolite of methamphetamine)	7–34 hours	
Heroin	60–90 minutes	In minutes
Morphine (metabolite of heroin)	1.3—6.7 hours	Opiates positive for 2–4 days (EIA)
6-Mono-acetyl-morphine (MAM)	30 minutes	Few hours
Phencyclidine (PCP)	7–16 hours	2–3 days
Cocaine	0.5–1.5 hours	Few hours
Benzoylecgonine (metabolite of cocaine)	5–7 hours	3–5 days
δ -Tetrahydrocannabinol	14–38 hours	90% fall in 1 hour (blood)
δ -Tetrahydrocannabinoic acid (marijuana metabolite in urine)		Depending on use, few days to many weeks
Benzodiazepines	Few hours to days	days to weeks, depending on half-life
Diazepam	15–40 hours	2 weeks
Flunitrazepam (rohypnol)	9–25 hours	0.2% excreted unchanged!
Methadone	15–40 hours In chronic patient ~22–24 hours	
Barbiturate (phenobarbital)	35–120 hours	1–2 weeks after last use
Alcohol (ethanol)	Blood levels fall by an average of 4–5 mmol/L/hour (15–18 mg/100 mL)/hour	1.5 > 12 hours depending on the peak blood level. Urine typically positive for an additional 1–2 hours.
Gamma-hydroxybutyrate (GHB)	0.3–1.0 hour	Less than 12 hours

The detection period is very much dose-dependent. The larger the dose, the longer the period the drug/metabolite can be detected in the urine.

Table 2. Drug half-lives and approximate urine detection periods. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

40mg/100mL. In Canada there are also two limits: 50mg/100mL and 80mg/100mL. BAC levels between 50mg/100mL and 80mg/100mL call for suspension of driving privileges but above 80mg/100mL are subject to criminal charges.

URINE TESTING METHODS

Urine is the most commonly used fluid for drug screening. The methods most commonly used in toxicology laboratories are: *immunoassay, chromatographic* and *chromatography coupled with mass spectrometry.* These methods vary considerably with respect to their sensitivity and reliability. Thin-layer chromatography is least expensive, gas chromatography coupled with mass spectrometry (GC/MS), which is considered as nearly perfect or "gold standard," is the most expensive. Table 2 summarizes the various methods.

Immunoassays (EIA, EMIT, FPIA, CEDIA and KIMS). Immunoassay methods are used for preliminary screening (i.e., initial screening). Since these methods are based on an antibody-antigen reaction, small amounts of the drug or metabolite(s) can be detected. Antibodies specific to a particular drug are produced by injecting laboratory animals with the drug. These antibodies are then tagged with markers such as an enzyme (enzyme immunoassay, EIA), a radio isotope (radioimmunoassay, RIA) or a fluorescence (fluorescence polarization immunoassay, FPIA) label. Reagents containing these labelled antibodies can then be introduced into urine samples, and if the specific drug against which the antibody was made is present, a reaction will occur. RIA is the oldest immunoassay method used to detect drugs. The major drawback of this method is that it requires a separation step and generates radioactive waste. RIA also requires special equipment to measure radioactivity.

Typically, immunoassays are designed for a *class* of drugs. Thus, their specificity (the ability to detect the presence of a *specific* drug) is not very good, since substances that have similar chemical structures will "cross-react" and give a false positive reaction. For example, the immunoassay method for cannabinoids was developed to detect the carboxylic acid metabolite of δ^9-THC. Yet, there is a suggestion in the literature that some nonsteroidal anti-inflammatory drugs, such as ibuprofen (a nonprescription drug in the U. S. and Canada) and naproxyn give random or sporadic false positive results for cannabinoids. Cough-syrup codeine will also give a positive reaction for the morphine (a

1. *Immunoassays*
   Enzyme immunoassay (EIA)
   Enzyme-multiplied immunoassay technique (EMIT)
   Fluorescence polarization immunoassay (FPIA)
   Radio immunoassay (RIA)
   Kinetic interaction of microparticles in solution (KIMS)
   Cloned enzyme donor immunoassay (CEDIA)
   Rapid slide tests (point-of-care testing)
2. *Chromatographic Methods*
   Thin-layer chromatography (TLC)
   Liquid chromatography (HPLC)
   Gas chromatography (GC)
3. *Chromatography/Mass Spectrometry*
   Gas chromatography/mass spectrometry (GC/MS)
   Liquid chromatography/mass spectrometry (HPLC/MS)

Table 3. Common drug-testing methods. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

metabolic product of heroin use) immunoassay and many antihistamines that are available over-the-counter may yield positive reactions for amphetamines. While some reagent manufacturers claim to have overcome many of these cross-reactivity problems, confirmation by a nonimmunoassay method is very important.

Urine test kits, designed to detect drugs, have been available in North America for the past few years. More recently, single and multiple test immunoassay kits designed for home and on-site testing have also been introduced. These kits generally carry a cautionary disclaimer that positive test results must be confirmed by the reference GC/MS method. When used in the non-laboratory environment, they are prone to procedural inaccuracies, poor quality control, abuse and misinterpretations. Therefore, these kits should be used with great caution. The risk of labelling a person with a false positive is high without the accompanying confirmatory analysis. Table 3 summarizes the advantages and disadvantages of immunoassay testing.

Chromatographic Methods. Separation of a mixture is the main outcome of the chromatographic method. For illustrative purposes, if one were to put a drop of ink on a blotting paper and hold the tip of the paper in water, one would observe the water rise in the paper. After a period of time and under the right conditions, the single ink spot would separate into many different compounds (spots) of different colors (blue ink is a mixture of many dyes). This process, where a mixture of substances is separated in a stationary medium (filter paper), is called chromatography. The types of chromatographic processes used in the analysis of drugs include thin-layer, gas, and liquid chromatography as well as a combination of gas or liquid chromatography with mass spectrometry.

Of the several chromatographic methods, thin layer chromatography (TLC) is the one most similar to the ink separation example mentioned previously. This method requires extensive sample preparation and technical expertise on the part of the analyst, but it is inexpensive and very powerful if used properly. With the exception of *Cannabis*, which requires separate sample preparation, a large number of drugs (e.g., cocaine, amphetamine, codeine, and morphine) can be screened at the same time. By combining different TLC systems, a high degree of specificity can be obtained, although the training of the analyst is crucial because of the subjectivity involved in interpreting the results. To identify positive TLC "spots," the technologist looks for the drugs and/or its metabolite pattern, often by spraying with reagents that react to form different colors with different drugs. The trained technologist can comfortably identify more than forty different drugs.

Similar to TLC, gas chromatography (GC) requires extensive sample preparation. In GC, the sample to be analyzed is introduced via a syringe into a narrow bore (capillary) column which sits in an oven. The column, which typically contains a liquid adsorbed onto an inert surface, is flushed with a carrier gas such as helium or nitrogen. (GC is also sometimes referred to as gas-liquid chromatography (GLC). In a properly set up GC system, a mixture of substances introduced into the carrier gas is volatilized, and the individual components of the mixture migrate through the column at different speeds. Detection takes place at the end of the heated column and is generally a destructive process. Very often the substance to be analyzed is "derivatized" to make it volatile or change its chromatographic characteristics.

In contrast to GC, high pressure liquid chromatography (HPLC), a liquid under high pressure, is used to flush the column rather than a gas. Typically, the column operates at room or slightly above room temperature. This method is generally used for

Advantages

1. Screening tests can be done quickly because automation and batch processing are possible.
2. Technologists doing routine clinical chemistry testing can be easily trained.
3. Detection limits are low and can be tailored to meet the program screening requirements. For example, lower detection thresholds can be raised to eliminate positives due to passive inhalation of marijuana smoke.
4. Immunoassays are relatively inexpensive, although the single-test kits can be very expensive when quality assurance and quality control samples are included.
5. Immunoassays do not require a specialized laboratory. Most clinical laboratories have automated instruments to do the procedures.

Disadvantages

1. Although the tests are useful for detecting classes of drugs, specificity for individual drugs is weak.
2. Since the antibody is generated from laboratory animals, there can be a lot-to-lot or batch-to-batch variation in the antibody reagents.
3. Results must be confirmed by another nonimmunoassay method.
4. A radioactive isotope is used in RIA that requires compliance with special licensing procedures, use of gamma counters to measure radioactivity, and disposal of the radioactive waste.
5. Only a single drug can be tested for at one time.

Table 4. Advantages and disadvantages of immunoassays. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

substances that are difficult to volatilize (e.g., steroids) or are heat labile (e.g., benzodiazepines).

Gas chromatography/mass spectrometry (GC/MS) is a combination of two sophisticated technologies. GC physically separates (chromatographs or purifies) the compound, and MS fragments it so that a fingerprint of the chemical (drug) can be obtained. Although sample preparation is extensive, when the methods are used together the combination is regarded as the "gold standard" by most authorities. This combination is sensitive, i.e., can detect low levels, is specific, and can identify all types of drugs in any body fluid. Furthermore, assay sensitivity can be enhanced by treating the test substance with reagents. When coupled with MS, HPLC/MS is the method of choice for substances that are difficult to volatilize (e.g. steroids).

Given the higher costs associated with CG/MS, urine samples are usually tested in batches for broad classes of drugs by immunoassays and positive screens are later subjected to confirmation by this more expensive technique.

Table 4 gives a summary of the advantages and disadvantages of each method of chromatographic drug testing and Table 5 compares all the methods of testing. The initial minimal immunoassay and GC/MS (cut-off) levels for five drugs or classes of drugs, as suggested by the U.S. National Institute of Drug Abuse, are listed in Table 6.

Procedures for Alcohol Testing. Since the introduction of the micro method for alcohol analysis in blood by Widmark in 1922, many new methods and modifications have been introduced. The distillation/oxidation methods are generally *non-specific* for alcohol (ethanol), whereas biochemical methods (spectrophotometric) using alcohol dehydrogenase (ADH) obtained from yeast and the gas chromatographic method that are currently used are specific for ethanol. The radiative attenuation energy technique and those using alcohol oxidase method are non-specific and will detect not only ethanol but also other alcohols. The recently introduced alcohol dipstick based on the ADH enzyme system is not only specific for ethanol, but also sensitive and does not require instrumentation. It can be used for the detection of ethanol in all body fluids and can provide semi-quantitative results in ranges of pharmacological-toxicological interest. Alcohol dipsticks are being used in a number of laboratories as a screening device.

Breath can be analyzed by using a variety of instruments. Most of the instruments used today detect ethanol by using thermal conductivity, colorimetry, fuel cell, infrared, or gas chromatography. Typically in most countries, local statutes define the instrument and method that can be used for evidenciary purposes. A variety of Breathalyser instruments ranging in costs from $100 to $1000 are available to do the test. These instruments are compact and portable. Canadian law enforcement authorities use the Breathalyser "Alert" which can give a "pass" or "fail" result as a roadside alcohol-screening device. The "failed" person is generally subjected to a "Borkenstein" Breathalyser to measure the BAC before any charges are brought. Many devices are available to preserve the breath sample for later analysis if a Breathalyser is not available

Advantages	
All the chromatographic methods are specific and sensitive and can screen a large number of drugs at the same time.	
TLC	Negligible capital outlay is needed.
GC	The procedure can be automated.
HPLC	Of the chromatographic procedures, this has the easiest sample preparation requirements. The procedure can be automated.
GC/MS	This is the "gold standard" test. Computerized identification of fingerprint patterns makes identification easy. The procedure can be automated. This is currently the preferred method for defense in the legal system.
Disadvantages	
All chromatographic methods are labor-intensive and require highly trained staff. Although the chromatographic methods are specific, confirmation is still desirable.	
TLC	Interpretation is subjective, hence, training and experience in interpretation capabilities of the technologist are crucial.
HPLC or GC	Equipment costs are high, ranging between $25,000 to $60,000, depending on the type of detector and automation selected (1994 $)
GC/MS	Equipment costs are the highest, ranging from $120,000 to $2000,000, depending on the degree of sophistication required (1994 $). Due to the complexity of the instrument, highly trained operators and technologists are required.

Table 5. Summary of chromatographic methods. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

immediately. In forensic laboratories, gas chromatography (North America) or biochemical procedures (many European countries) are used to analyze biological samples.

Blood samples that cannot be analyzed soon after collection should have sodium fluoride (NaF) added as a preservative. Alcohol dehydrogenase (ADH), the enzyme responsible for the oxidation of alcohol, is also present in the red blood cell and will slowly metabolise the alcohol, causing its concentration to drop if the preservative is not added. Large amounts of alcohol can be produced *in-vitro* in the urine samples of diabetic patients if samples are not processed immediately or properly preserved.

INTERPRETATIONS OF TEST RESULTS

False Negatives. A positive or negative result is highly dependent on the sensitivity of the drug detection method. A false negative occurs when the drug is present but is not found because the detection limit of the method used is too high or the absolute quantity of the drug in the specimen is too low.

Large amounts of fluids consumed prior to obtaining a sample for analysis can affect detection of drugs in urine samples. Under conditions of dilution, although the absolute amount of drug or metabolite excreted may be the same over a period of time, the final concentration per milliliter will be reduced and may give a false negative result. Acidity levels in the urine may also affect the excretion of the drug into the urine. In some cases elimination is enhanced, whereas in other cases, the drug is reabsorbed.

Several measures can be used to decrease the likelihood of obtaining a false negative result. First, sensitivity of the method can be enhanced by analyzing for the drugs' metabolites. Heroin use, for example, is determined by the presence of its metabolite, morphine. Increasing the specimen volume used for analysis or treating it with chemicals can also make laboratory methods more sensitive. Studies have shown that a 5-mg dose of Valium® is usually detected for three to four days; however, when these improved methods are utilized, sensitivity can be increased, such that, the same dose can be detected for up to 20 days. One important drawback of such high sensitivities is, that estimates of when the drug was taken are far less accurate.

False Positives. A false positive occurs when results show that the drug is present, when in fact it is not. False-positive tests are obtained if an interfering drug or substance is present in the biological fluid and it cross-reacts with the reagents. An example of this is Daypro (oxaprozin) will give a false positive for benzodiazepines. Other substances may have a metabolite that will give a positive reaction. An example of this is Selegiline, an anti-Parkinson drug, which has amphetamine as one of its metabolites. Although this would be analytically a true positive, it is a false positive from a drug abuse perspective. As discussed in the previous section on immunoassay, an initially positive test based on an immunoassay technique should always be confirmed with an nonimmunoassay method. A confirmed positive finding only implies that the urine sample contains the detected drug and nothing more.

Test	Initial test	Confirmatory test
Marijuana metabolite[1]	50 ng/mL	15 ng/mL
Cocaine metabolites[2]	300 ng/mL	150 ng/mL
Opiate metabolites	2,000 ng/mL	
Morphine		2,000 ng/mL
Codeine		2,000 ng/mL
6-Acetylmorphine[3]		10 ng/mL
Phencyclidine (PCP)	25 ng/mL	25 ng/mL
Amphetamines	1,000 ng/mL	
Amphetamine		500 ng/mL
Methamphetamine[4]		500 ng/mL

[1]Delta-9 THC carboxylic acid
[2]Benzoylecgonine
[3]Test for 6-AM when the morphine concentration is greater than or equal to 2,000 ng/mL
[4]Specimen must also contain amphetamine at a concentration greater than or equal to 200 ng/mL

Table 6. Cut-off levels for initial and confirmatory rests. (Source: HHS Mandatory Guidelines, November 1, 2004. Division of Workplace Programs, Substance Abuse and Mental Health Administration, U.S. Department of Health and Human Services.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

	EMIT FPLA	RIA	TLC	GC HPLC	GC/MS
Ease of sample preparation	X	X		X	
Less highly trained technologists required	X	X			
Limited equipment required	X	X	X		
Low detection limits	X	X	X	X	X
Adjustable lower threshold	X	X			
Highly specific and sensitive			X	X	X
Computerized identification possible					X
Screen for several drugs at a time			X	X	X
Procedure can be automated	X	X		X	X
Special atomic energy license required		X			
Confirmation of results required	X	X	X	X	
Interpretation is subjective			X		

Table 7. Comparison of all testing methods. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

At times false positives are attributable to ingested substances such as allergy medications. Some authors have suggested that employees subject to drug screening refrain from using popular over-the-counter medications, such as Alka-Seltzer Plus and Sudafed, because they have caused false-positives. Some natural substances such as herbal teas and poppy seeds can also give positive responses to screens. These may be analytically true positives but need to be distinguished from those due to illegal drug use. In some instances, false-positives have been due to mistakes or sabotage of the chain of custody for urine samples.

COMMON ADULTERATION METHODS

The method of switching "clean" urine for "dirty" urine; resubmitting one's own or urine that is provided by someone else are the most common ways to fool the drug screening system. A number of entrepreneurs have attempted to bypass urine-specimen inspection by substituting clean urine. For example, a company in Florida sells lyophilized (freeze dried) clean urine samples through newspaper and magazine advertisements. Hiding condoms containing "clean" urine on the body or inside the vagina is another common trick.

Some have substituted apple juice and tea in samples for analysis. Patients are known to add everything from bleach, liquid soap, eye-drops, and many other household products, hoping that their drug use will be masked. Others may hide a masking substance under their fingernails and release it into the urine specimen. Another method is to poke a small hole into the container with a pin so that the sample leaks out by the time it reaches the laboratory.

Since addition of table salt (NaCl) or bleach to the urine is a common practice, many laboratories routinely test for Na and Cl in the urine. Liquid soap and crystalline drain cleaners that are strong alkaline products containing sodium hydroxide (NaOH) are also used to adulterate the urine sample. These contaminators can be detected by checking for high levels of pH in the urine sample. In-vivo alkalizing or acidifying the urine pH can also change the excretion pattern of some drugs including amphetamines, barbiturates and phencyclidine (PCP).

Water-loading (drinking large amounts of water prior to voiding) poses an interesting challenge to testing laboratories. Specific gravity has been used to detect dilution; however, the measurement range is limited so it is not yet useful. Creatinine levels on random urine samples appear to be a promising method for detection of water-loading. A number of adulteration methods are being advertised on the Internet. Invariably, one of the instructions for adulteration is to drink copious amounts of fluids to bring about *in-vivo* dilution or water-loading. Some Internet sites even sell adulterants that can be added to the urine.

Typically these products either try to oxidise the drug present or try to change the pH of the urine to interfere with the analytical method. Most of the laboratories involved in drug testing routinely test for the various adulterants. To detect resubmitted samples, a "urine fingerprinting" method using dietary components has been described.

Drug users are very resourceful and their ingenuity should not be underestimated. To reduce the opportunities for specimen contamination, some workplaces require that employees provide a urine sample under direct supervision. Another technique used to detect any sample adulteration is to take the temperature of the sample. In a study, Kapur et al. (1993) took the temperature of urine samples when taken within one minute of voiding; it fell between 36.5°C and 34 degrees Celsius, reflecting the inner body core temperature. It is very difficult to achieve this narrow temperature range by hiding a condom filled with urine under the armpit or adding water from a tap or toilet bowl to the urine sample. It is important that the temperature of the specimen be measured immediately after the sample is taken, since it can drop rapidly.

LABORATORY PROCEDURAL AND SECURITY STANDARDS

It is important that the laboratory drug testing facility has qualified individuals who follow a specific set of laboratory procedures and meet recommended security standards.

DRUG TESTING METHODS AND CLINICAL INTERPRETATIONS OF TEST RESULTS: SUMMARY AND CONCLUSION

In this paper, major issues related to drug testing are discussed. For example, drug-testing techniques measure drug presence but are not sophisticated enough to measure impairment from drug use. It is also very difficult to determine the route of drug administration, quantity, frequency, or when the drug was last taken.

Selection of the drug to be tested should depend on the local availability of the drug, its abuse potential, and clinical effects, as well as the available analytical technology and expertise in testing and interpretation of the laboratory results. The most sophisticated drug-testing approach, gas chromatography in combination with mass spectrometry, is considered as a gold standard and thus utilized in confirmatory testing. Typically GC/MS is preceded by a rapid immunoassay method to eliminate the majority of negative samples.

Despite the existence of sophisticated drug-testing methods, incorrect test results can still occur. These can be due to the presence of interfering substances or adulteration of the urine sample. Patients have been known to adulterate urine samples to avoid drug detection. A number of techniques can be employed to reduce the likelihood of obtaining erroneous results, as well as detect adulterated urine samples. "Positive" drug finding can have a serious impact on the livelihood of an individual, therefore the performance of these tests should adhere to the strictest laboratory standards of performance. Only qualified and experienced individuals with proper laboratory equipment should perform these analyses. Standards of laboratory performance must meet local legal and forensic requirements. Access to the patient samples as well as laboratory records must be restricted in order to prevent tampering with samples and results. To maintain confidentiality and assure proper interpretation of results, the results must be communicated only to the physician reviewing the case/patient. Chain of custody and all documents pertaining to the urine sample must be maintained so that they can be examined in case of a legal challenge. The laboratory must have a complete record on quality control. Finally, specific initial and confirmatory testing requirements should be met.

See also **Blood Alcohol Concentration; Breathalyzer; Hair Analysis as a Test for Drug Use.**

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DRUG TYPES. The various types of drugs that are used and abused by humans for nonmedical purposes can be divided into several major categories, based upon their general pharmacological and subjective effects. These categories include: ethanol, nicotine and tobacco, central nervous system depressants, central nervous system stimulants, cannabinoids, opioids, psychedelics, inhalants, and arylcyclohexylamines. Although the mechanisms of action may vary among the drugs within a single category, the general effects of the drugs in each category are similar. The drugs in each category are described below in terms of their pharmacology, abuse, dependence, and withdrawal, as well as their toxicity. The legal and readily available drugs (i.e., alcohol and tobacco) are described first, because the use and abuse of these drugs is more widespread than that of all of the other categories of abused drugs combined. The health problems associated with the chronic use of alcohol and tobacco are, therefore, a far-reaching problem in modern society, not only because of the vast numbers of people who suffer and die each year due to the toxic effects of these substances, but also because of the financial drain they impose due to absenteeism from work and increased health-care costs.

Prescription drugs are covered next, and then the illegal drugs are discussed. Although the illicit use of heroin, cocaine and other drugs remains a major social, legal, financial, and health problem in the United States, the percentage of the population physically dependent on these drugs is relatively low when compared to legal drugs that are abused. Finally, it is important to take into consideration the fact that individuals often do not restrict their drug use to drugs within a single category. Alcoholics typically smoke cigarettes, and they often use benzodiazepines as well. Many heroin users also smoke, and they may consume alcohol and other sedatives, cannabis, or stimulants. Multiple drug use is, therefore, a relatively common occurrence among individuals who use drugs for their subjective, nonmedical effects.

ALCOHOL

Although alcohol has been used throughout recorded history, it is generally accepted that the therapeutic value of ethanol is extremely limited and that chronic alcoholism is a major social and medical problem. Approximately two-thirds of all adults in the United States use alcohol occasionally. Hundreds of thousands of individuals suffer and die each year from complications associated with chronic alcoholism, and tens of thousands of innocent individuals are injured or killed each year in alcohol-related traffic accidents. Thus, alcoholism is a far-reaching problem, affecting the lives of individuals who consume ethanol as well as those who do not.

Although alcohol is considered by many people to be a stimulant drug because it typically releases an individual's latent behavioral inhibitions, alcohol actually produces a powerful primary and continuous depression of the central nervous system, similar to that seen with general anesthetics. In general, the effects of alcohol on the central nervous system are proportional to the blood (and brain) concentrations of the drug. Initially, memory and the ability to concentrate decrease and mood swings become more evident. As the level of intoxication increases, so does the impairment of nervous function, until a condition of general anesthesia is reached. However, there is little margin of safety between an anesthetic dose of ethanol and severe respiratory depression.

In chronic alcoholism, brain damage, memory loss, sleep disturbances, psychoses, and increased seizure susceptibility often occur. Chronic alcoholism is also one of the major causes of cardiomyopathy (impaired function of the heart muscle) in the United States due to irreversible ethanol-induced damage to that tissue. Ethanol also stimulates the secretion of gastric acid in the stomach, and it can produce ulcers of the stomach and intestine. One of the primary metabolic products of ethanol is acetaldehyde, which is toxic. In chronic alcoholism, acetaldehyde can accumulate in the liver, resulting in hepatitis and cirrhosis of the liver. Finally, the long-term use of alcohol can result in a state of physical dependence.

With relatively low levels of dependence, withdrawal from alcohol may be associated with problems such as sleep disturbances, anxiety, weakness, and mild tremors. In more severe dependence, the alcohol withdrawal syndrome can include more pronounced tremors, seizures, and delirium, as well as a number of other physiological and psychological

effects. In some cases, this withdrawal can be life threatening. Because alcohol has cross-tolerance with other central nervous system depressants, benzodiazepines or barbiturates can be successfully used to decrease the severity of the alcohol withdrawal syndrome. Longer-acting benzodiazepines and related drugs can be used as an ethanol substitute, and the dose of the benzodiazepine can then be gradually reduced over time to attenuate or prevent the occurrence of convulsions and other potentially life-threatening toxic reactions generally associated with alcohol withdrawal.

As outlined above, the chronic use of ethanol can result in a wide range of toxic effects on a variety of organ systems. However, the mechanisms through which ethanol produces its varied effects are not clearly understood. The anesthetic or central nervous system depressant effects may result, in part, from general changes in the function of ion channels that occur when ethanol dissolves in lipid membranes. Other research suggests that alcohol may interact with specific binding sites associated with the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), in a manner somewhat analogous to other central nervous system depressants (e.g., benzodiazepines or barbiturates). However, because an ethanol receptor site has not yet been conclusively identified, specific receptor agonists and antagonists are not yet available for the treatment of ethanol intoxication or withdrawal, or for the maintenance of abstinence.

Disulfiram is sometimes used in the treatment of chronic alcoholism, although the drug does not cure alcoholism. Rather, disulfiram interacts with ethanol to alter the intermediate metabolism of ethanol, resulting in a five- to tenfold increase in plasma acetaldehyde concentrations. This acetaldehyde syndrome results in vasodilatation, headache, breathing difficulties, nausea, vomiting, sweating, faintness, weakness, and vertigo. Thus, it helps persuade alcoholics to remain abstinent, because they realize that they cannot drink ethanol for up to two weeks after taking disulfiram. More recently, naltrexone was approved as the first agent for the pathological reward and reinforcement effects of alcohol. Naltrexone is an opioid receptor antagonist that appears to reduce these responses in alcoholics via the endogenous opioid system. Oral naltrexone has demonstrated efficacy and safety in the treatment of alcohol dependence in controlled clinical trials. A long-acting injectable formulation of naltrexone has also been approved for use in the United States. Finally, acamprosate, a medication first evaluated in Europe, has also been approved for use in the United States. This medication acts on both GABA and glutamate (an excitatory neurotransmitter) to maintain abstinence in alcohol-dependent individuals.

TOBACCO

Tobacco was first introduced to Europe by the crews that accompanied Christopher Columbus to the "New World." By the middle of the nineteenth century, tobacco use had become widespread. Although tobacco use has declined dramatically in recent years, 18 to 24 percent of the adults in the United States are still regular tobacco smokers. This relatively high use of tobacco exists despite the large body of scientific evidence linking cigarette smoking to numerous life-threatening health disorders, including lung cancer and heart disease. The constituents of tobacco smoke that are most likely to contribute to these health problems include carbon monoxide, nicotine, and "tar."

Nicotine is the primary component of tobacco smoke that promotes smoking. Nicotine facilitates memory, reduces aggression, and decreases weight gain. Each of these effects could, by itself, provide a rationale for continued tobacco use, as most individuals find increased alertness and memory, decreased irritability, and decreased weight gain to be positive effects. However, these effects may actually be secondary to the primary reinforcing effects of nicotine itself. In laboratory settings, smokers report that the intravenous injection of nicotine produces a pleasant feeling on its own. However, nicotine causes unpleasant effects in nonsmokers, often resulting in dizziness, nausea, and vomiting. Tolerance to these unpleasant effects develops rapidly, however. Although nicotine obviously binds to nicotinic receptors associated with the neurotransmitter acetylcholine, there is evidence that the reinforcing or rewarding properties of nicotine may result from an activation of ascending limbic neurons that release the neurotransmitter dopamine (i.e., in the mesocorticolimbic dopaminergic system, which has been implicated in the reinforcing properties of a variety of drugs, including stimulants and opiates).

As stated above, tobacco smoking has been associated with a wide variety of serious health effects, including cancer and heart disease. However, the chances of developing these health problems decrease once smoking is terminated. Although some of the smoking-induced damage is irreversible, the incidence rates for cancer and heart disease gradually become more similar to that of nonsmokers the longer that the smoker refrains from smoking. However, those who quit smoking experience a withdrawal syndrome that varies in intensity from individual to individual and often leads to a relapse. This syndrome consists of a craving for tobacco, irritability, weight gain, difficulty concentrating, drowsiness, and sleep disturbances. The introduction of nicotine replacement therapy (in the form of chewing gum, transdermal patches, nasal spray, inhalers, tablets, or lozenges) has significantly helped to sustain abstinence from smoking in a number of individuals by delivering nicotine in a less toxic way. The orally administered medications varenicline and bupropion, which are not nicotine replacement therapies, are also regarded as first-line treatments, either used alone or as an adjunct to nicotine replacement therapy. Second-line treatments include clonidine and nortriptyline. Other treatment strategies that have been examined include monoamine oxidase inhibitors (MAOIs) and selective serotonin-reuptake inhibitors (SSRIs), but efficacy has yet to be proven definitively for these medications. A novel approach to treatment using the cannabinoid-1 receptor antagonist rimonabant is also under investigation.

CENTRAL NERVOUS SYSTEM DEPRESSANTS

Central nervous system depressants include barbiturates, benzodiazepines, and related drugs. Receptor binding sites for benzodiazepines and barbiturates are part of a macromolecular complex associated with chloride ion channels and the inhibitory neurotransmitter GABA. The interaction of these drugs with their distinct binding sites results in a facilitation of GABAergic neurotransmission, producing an inhibitory effect on neuronal impulse flow in the central nervous system. The shorter-acting barbiturates such as pentobarbital ("yellow jackets") or secobarbital ("red devils") are usually preferred to the longer-acting drugs such as phenobarbital. Nonbarbiturates such as meprobamate, glutethimide, methyprylon, and methaqualone (Quaalude) are also abused, though these medications are not as widely available as they were before the introduction of the benzodiazepines. Some of the shorter-acting benzodiazepines are also abused, providing evidence that the quicker the onset of action for a particular central nervous system depressant, the better the "high."

There is no general rule that can be used to predict the pattern of use of a central nervous system depressant for a given individual. There is often a fine line between the appropriate therapy for insomnia or anxiety and drug dependence. Some individuals exhibit cyclic patterns of abuse, with gross intoxication for a few days interspersed with periods of abstinence. Other barbiturate or benzodiazepine users maintain a chronic low level of intoxication without any observable signs of impairment. Such individuals have developed a tolerance to many of the side effects of these drugs. When higher doses are used, however, the intoxication may resemble alcohol intoxication, with slurred speech, difficulty thinking, memory impairment, sluggish behavior, and emotional instability. Withdrawal from chronic barbiturate or benzodiazepine use can also be manifested to varying degrees. In the mildest form, the individual may only experience mild anxiety or insomnia. With greater degrees of physical dependence, tremors and weakness may also occur. In severe withdrawal, delirium and tonic-clonic seizures may also be present. This severe withdrawal syndrome can be life threatening. The degree of severity of the withdrawal syndrome appears to be related to the pharmacokinetics of the drug used. For example, shorter-acting benzodiazepines and barbiturates produce much more severe cases of withdrawal than the longer-acting drugs. Therefore, in the case of severe withdrawal symptoms associated with the chronic use of a short-acting drug, a longer-acting drug should be substituted. The dose of this longer-acting drug can thus be gradually decreased so that the individual experiences a much milder and less threatening withdrawal.

CENTRAL NERVOUS SYSTEM STIMULANTS

Central nervous system stimulants include caffeine, cocaine, and amphetamine. Perhaps 80 percent of the world's population ingests caffeine in the form of tea, coffee, cola-flavored drinks, or chocolate. In the central nervous system, caffeine decreases drowsiness and fatigue and produces a more rapid and clearer flow of thought. With higher doses,

however, nervousness, restlessness, insomnia, and tremors may result. Cardiac and gastrointestinal disturbances may also be seen. Tolerance typically develops to the anxiety and dysphoria (negative mood) experienced by some individuals. However, some degree of physical dependence has been associated with the chronic consumption of caffeine. The most characteristic symptom of caffeine withdrawal is a headache, although fatigue, lethargy, and some degree of anxiety are also common. In general, the long-term consequences of chronic caffeine consumption are relatively minor. On the other hand, the problems associated with chronic cocaine and amphetamine use and withdrawal are much more serious.

More than 20 million people have used cocaine in the United States alone. Following the introduction of cocaine in the free alkaloid base ("freebase" or "crack") form, there was a significant increase in cocaine-related medical, economic, social, and legal problems. In the freebase form, cocaine can be smoked, resulting in blood levels and brain concentrations of the drug that compare to those observed when the drug is injected intravenously. In normal subjects in a laboratory setting, the administration of cocaine or amphetamine produces an elevation of mood, an increase in energy and alertness, and a decrease in fatigue and boredom. In some individuals, however, anxiety, irritability, and insomnia may be observed. In non-laboratory settings, heavy users of cocaine often take the drug in bouts or binges, only stopping when their supply runs out or they collapse from exhaustion. Immediately following the intravenous administration or inhalation of cocaine, the individual experiences an intense pleasurable sensation known as a "rush" or "flash," that is followed by a sense of euphoria. Cocaine rapidly penetrates into the brain to produce these effects, but it is then rapidly redistributed to other tissues. In many cases, the intense pleasure followed by the rapid decline in the cocaine-induced elevation of mood is sufficient for the individual to begin immediately to seek out, procure, and use more of the drug to prolong these pleasurable effects. With the intranasal administration of cocaine, the pleasure is less intense and the decline in brain concentrations is much slower, so that the craving for more of the drug is less pronounced.

Cocaine and amphetamine appear to produce their reinforcing or pleasurable effects through interactions with the neurotransmitter dopamine, especially in the limbic and cortical regions of the brain (i.e., within the mesocorticolimbic dopaminergic system). Both cocaine and amphetamine block the reabsorption of dopamine into the neurons where it was released, thereby prolonging the action of dopamine in the synapse (the space between nerve cells). Amphetamine can also cause the direct release of dopamine from nerve cells, and it can inhibit the metabolism of the neurotransmitter. It is important to note, however, that every drug that augments the action of dopamine does not produce pleasurable or rewarding subjective effects. Toxicity associated with cocaine or amphetamine use can be quite severe and is often unrelated to the duration of use or to any preexisting medical conditions in the individual. This potential for serious toxic side effects is amplified by the fact that tolerance usually develops to the subjective feelings of the cocaine-induced rush and euphoria, but not to some of the other central nervous system effects of the drug, especially seizure susceptibility.

Some of the more minor toxic reactions include dizziness, confusion, nausea, headache, sweating, and mild tremors. These symptoms are experienced by virtually all cocaine and amphetamine users to some degree as a result of the stimulation of the sympathetic nervous system. However, more serious reactions are also frequently observed, including irregular heartbeats, convulsions and seizures, heart attack, liver failure, kidney failure, heart failure, respiratory depression, stroke, coma, and death. The effects on the heart and vascular system can sometimes be treated with alpha- and beta-noradrenergic receptor antagonists or calcium channel blockers, although even prompt medical attention is not always successful. The convulsions can sometimes be controlled with diazepam, and ventilation may be required for the respiratory depression.

In addition to the effects described above for cocaine, amphetamine has been reported to produce direct and irreversible neuronal damage to dopaminergic and nondopaminergic neurons. A similar effect for cocaine has not yet been identified. Psychiatric abnormalities resulting from chronic central nervous system stimulant abuse can include anxiety, depression, hallucinations, and, in some

cases, a paranoid psychosis that is virtually indistinguishable from a paranoid schizophrenic psychosis.

A withdrawal syndrome is also observed following the abrupt cessation of chronic cocaine or amphetamine use. This syndrome begins with exhaustion during the "crash" phase and is followed by prolonged periods of anxiety, depression, anhedonia (reduced capacity to experience pleasure), hyperphagia (voracious eating), and an intense craving for the drug that may persist for several weeks, depending on the individual. The administration of dopaminergic agonists or tricyclic antidepressants may have some utility in decreasing the severity of withdrawal symptoms, which could reduce the risk of relapse. More recently, however, a number of novel targets for cocaine pharmacotherapy have emerged. Disulfiram, a medication with dopaminergic effects, has been reported to reduce cocaine use in a number of clinical trials, as have GABA medications, such as tiagabine and topiramate. A beta-adrenergic blocker, propranolol, may also be effective, especially among cocaine-addicted individuals with high withdrawal severity. Treatment with modafinil, a stimulant medication, has also been reported to reduce cocaine use. Finally, a cocaine vaccine that slows entry of cocaine into the brain by binding cocaine in the bloodstream may eventually hold promise. However, there is no FDA-approved medication for the treatment of dependence on cocaine, amphetamine or related drugs.

CANNABINOIDS

Marijuana, or cannabis (commonly referred to as "grass," "weed," or "pot"), is still the most commonly used illicit drug in the United States, with about 55 percent of young adults reporting some experience with the drug during their lifetimes. The active ingredient in marijuana is δ^9-tetrahydrocannabinol (δ^9-THC), which exerts its most prominent effects on the central nervous system and the cardiovascular system. A marijuana cigarette containing approximately 2 percent δ^9-THC produces an increase in feelings of well-being or euphoria and relaxation. Short-term memory is impaired, however, as is the ability to carry out goal-directed behavior, such as driving or operating machinery, effects that often persist for much longer than the subjective effects. With higher doses, paranoia, hallucinations, and anxiety or panic may be manifested. Chronic marijuana users sometimes exhibit what is called the "amotivational syndrome," which consists of apathy, impairment of judgment, and a loss of interest in personal appearance and the pursuit of conventional goals. However, it is not clear whether this syndrome results from the use of marijuana alone or from other factors. δ^9-THC also produces a dose-related increase in heart rate, although this is seldom severe. Tolerance develops to the effects of marijuana, and in some countries, regular users of hashish (a concentrated resin containing high levels of δ^9-THC) consume quantities of the drug that would be toxic to most marijuana users in the United States. The withdrawal associated with the cessation of marijuana smoking is relatively mild and consists of irritability, restlessness, nervousness, insomnia, weight loss, chills, and increased body temperature.

The endogenous cannabinoid system—called the endocannabinoid system—was discovered in the 1980s, and the compounds that modify this system are currently being reconsidered for their therapeutic potential. Thus, the term *cannabinoid* includes the numerous synthetic cannabinoids obtained by modifications of plant-derived cannabinoids or from the compounds that behave as endogenous ligands for the different cannabinoid receptor types. The term also refers to some prototypes of selective antagonists for these receptors. The explanation for this exponential growth in cannabinoid pharmacology is the discovery and characterization of the endocannabinoid signaling system (receptors, ligands, and inactivation system), which plays a modulatory role mainly in the brain, but also in the periphery. The endocannabinoid system is currently under investigation, not only for its role in marijuana dependence, but also for its ability to mediate dependence on other drugs, such as cocaine.

OPIOIDS

According to the 2005 Monitoring the Future Survey, the use of opioids in the United States is much less prevalent than the other drugs discussed above. Data suggest that less than 1.5 percent of young adults have reported trying heroin at some time during their lives, although the incidence of prescription opioid abuse is on the increase. There are three basic patterns of opioid use and dependence

in the United States. The smallest percentage of opioid users includes those individuals who initially began using morphine-like drugs medically for the relief of pain. A second group began using these drugs through experimentation and then progressed to chronic use and dependence. A third group comprises physically addicted individuals who eventually switched to oral methadone obtained through organized treatment centers. Interestingly, the incidence of opioid addiction is greater among physicians, nurses, and related health-care professionals than among any other group with a comparable educational background. In many instances, individuals addicted either to heroin purchased illegally on the street or to methadone are able to hold jobs and raise a family. Opioids reduce pain, aggression, and sexual drives, so that the use of these drugs is unlikely to induce crime. Obviously, however, other individuals (e.g., "junkies") are unable or unwilling to hold a job and resort to crime to support their drug habit.

Opioid drugs produce their pharmacological effects by binding to opiate receptors. The euphoria associated with the use of opioids results from the interaction of these drugs with the μ-opiate (or mu-opiate) receptor, possibly resulting in the stimulation of mesocorticolimbic dopaminergic neuronal activity. The rapid intravenous injection of morphine (or heroin, which is converted to morphine once it enters the brain) results in a warm flushing of the skin and sensations in the lower abdomen that are often described as being similar in intensity and quality to sexual orgasm. This initial "rush" (or "kick" or "thrill") lasts for about 45 seconds and is followed by a "high" that has been described as a state of dreamy indifference. Depending on the individual, good health and productive work are not incompatible with the regular use of opioids. Tolerance can develop to the analgesic, respiratory depressant, sedative, and reinforcing properties of opioids, but the degree and extent of tolerance depends largely on the pattern of use. The desired analgesia can often be maintained through the intermittent use of morphine. Tolerance develops more rapidly with more continuous opioid administration.

The abrupt discontinuation of opioid use can lead to a withdrawal syndrome that varies in degree and severity, depending on both the individual and the particular opioid used. Watery eyes (lacrimation), a runny nose (rhinorrhea), yawning, and sweating occur within 12 hours of the last dose of the opioid. As the syndrome progresses, dilated pupils, anorexia, gooseflesh ("cold turkey"), restlessness, irritability, and tremors can develop. As the syndrome intensifies, weakness and depression are pronounced, and nausea, vomiting, diarrhea, and intestinal spasms are common. Muscle cramps and spasms, including involuntary kicking movements ("kicking the habit"), are also characteristic of opioid withdrawal. However, seizures do not occur and the withdrawal syndrome is rarely life threatening. Without treatment, the morphine-induced withdrawal syndrome usually runs its course within 7 to 10 days.

Opiate receptor antagonists (e.g., naloxone) are contraindicated in opioid withdrawal as these drugs can precipitate a more severe withdrawal on their own. Rather, longer-acting and less potent opiate receptor agonists such as methadone are more commonly prescribed. The symptoms associated with methadone withdrawal are milder, although more protracted, than those observed with morphine or heroin. Therefore, methadone therapy can be gradually discontinued in some heroin-dependent individuals. If the patient refuses to withdraw from methadone, the individual can be maintained on methadone more or less indefinitely. In addition, a high-affinity partial μ agonist, buprenorphine, has been demonstrated to be as effective as methadone in the treatment of heroin dependence, with significantly better opiate abuse control. This treatment may therefore allow for longer and more effective treatment programs with reduced relapse rates.

PSYCHEDELICS

The psychedelics include drugs related to the indolealkylamines, such as lysergic acid diethylamide (LSD), psilocybin, psilocin, dimethyltryptamine (DMT), and diethyltryptamine (DET); to the phenylethylamines (e.g., mescaline); or to the phenylisopropylamines, such as 2,5-dimethoxy-4-methylamphetamine (DOM, or "STP"), as well as 3,4-methylenedioxyamphetamine (MDA) and 3,4-methylenedioxymethamphetamine (MDMA, or "Ecstasy"). According to the National Institute on Drug Abuse, in 2004, 9.7 percent of Americans aged 12 and older reported using LSD at least once in their lifetimes, while 0.2 percent had used it in the

past year, and 0.1 percent had used it in the past month. Lifetime use declined significantly from 2003 to 2004 among persons aged 12 to 17 and 18 to 25. Also according to the National Institute on Drug Abuse, an estimated 450,000 people in the United States aged 12 and older reported having used MDMA in the previous 30 days. MDMA use dropped significantly among persons 18 to 25—from 14.8 percent in 2003 to 13.8 percent in 2004 for lifetime use, and from 3.7 percent to 3.1 percent for past-year use. The feature that distinguishes these psychedelic agents from other classes of drugs is their capacity to reliably induce states of altered perception, thought, and feeling. There is a heightened awareness of sensory input accompanied by an enhanced sense of clarity, but there is also a diminished control over what is experienced. The effects of LSD and related psychedelic drugs appear to be mediated through a subclass of receptors associated with the inhibitory neurotransmitter serotonin (i.e., serotonin $5HT_2$ receptors). Immediately after the administration of LSD, somatic symptoms such as dizziness, weakness, and nausea are present, although euphoric effects usually predominate. Within two to three hours, visual perceptions become distorted; for example, colors are heard and sounds may be seen. Vivid visual hallucinations are also often present. Many times this loss of control is disconcerting to the individual, resulting in the need for structure in the form of experienced companions during the "trip." The entire syndrome begins to clear after about 12 hours. However, there is little evidence of long-term changes in personality, beliefs, values, or behavior produced by the drug. Tolerance rapidly develops to the behavioral effects of LSD after three or four daily doses of the drug. In general, however, the psychedelic drugs do not give rise to patterns of continued use over extended periods. The use of these drugs is generally restricted to the occasional "trip."

Withdrawal phenomena are not observed after the abrupt discontinuation of LSD-like drugs, and no deaths directly related to the pharmacological effects of LSD have been reported. However, other drugs chemically similar to MDMA, such as MDA (methylenedioxyamphetamine, the parent drug of MDMA) and PMA (paramethoxyamphetamine, which has been associated with fatalities in the United States and Australia) are sometimes sold as MDMA. These drugs can be neurotoxic or create additional health risks to the user. MDMA tablets may also contain other substances in addition to MDMA, such as ephedrine (a stimulant), dextromethorphan (DXM, a cough suppressant that has PCP-like effects at high doses), ketamine (an anesthetic used by veterinarians that also has PCP-like effects), caffeine, cocaine, and methamphetamine. While the combination of MDMA with one or more of these drugs may be inherently dangerous, users also combine them with substances such as marijuana and alcohol, putting themselves at further physical risk.

INHALANTS

The intoxicating and euphorigenic properties of nitrous oxide and ethyl ether were well known even before their potential as anesthetics was recognized. Physicians, nurses and other health-care professionals have been known to inhale anesthetic gases, even though they have access to a wide variety of other drugs. Adolescents with restricted access to alcohol often resort to "glue sniffing" or the inhalation of vapors from substances with marked toxicity such as gasoline, paint thinners, or other industrial solvents. The alkyl nitrites (butyl nitrite, isobutyl nitrite, and amyl nitrite) have been used as aphrodisiacs because the inhalation of these agents is thought to intensify and prolong orgasm. More than 17 percent of young adults have reported some experience with inhalants. However, fatal toxic reactions (usually due to cardiac arrhythmias) are often associated with the inhalation of many of these drugs. Inhalation from a plastic bag can result in hypoxia as well as an extremely high concentration of vapor; fluorinated hydrocarbons can produce cardiac arrhythmias and ischemia; chlorinated solvents depress myocardial contractility; and ketones can produce pulmonary hypertension. Neurological impairment can also occur with a variety of solvents.

ARYLCYCLOHEXYLAMINES

Arylcyclohexylamines include phencyclidine (PCP, or "angel dust") and related drugs that possess central nervous system stimulant and depressant effects and hallucinogenic and analgesic properties. These drugs (also known as dissociative anesthetics) are well absorbed using all methods of administration. Even small doses can produce an intoxication characterized by staggering gait, slurred speech, and numbness in the extremities. PCP users may also exhibit sweating, catatonia, and

a blank stare, as well as hostile and bizarre behavior. Amnesia during the intoxication may also occur. In higher doses, anesthesia, stupor, convulsions, and coma may appear. The typical "high" from a single dose can last four to six hours and is followed by a prolonged period of "coming down." PCP and related compounds bind with high affinity to a number of distinct sites in the central nervous system, although it is not certain which site (or sites) is responsible for the primary pharmacological effects of these drugs. PCP binds to the sigma site, which also has a high affinity for opioids. PCP also blocks the cation channel (e.g., Ca^{2+}) that is regulated by N-methyl-D-aspartate (NMDA), one type of receptor for excitatory amino acid neurotransmitters such as glutamate or aspartate. PCP also blocks the reabsorption of the neurotransmitter dopamine into the neurons from which it was released, resulting in a prolonged action of the neurotransmitter, especially within the mesocorticolimbic dopaminergic neuronal system.

There appears to be some degree of tolerance to the effects of PCP, and some chronic users of PCP complain of cravings and difficulties with recent memory, thinking, and speech after discontinuing the use of the drug. Personality changes following repeated use can range from social withdrawal and isolation to severe anxiety, nervousness, and depression. Although the frequency is uncertain, deaths due to direct toxicity, violent behavior, and accidents have been reported following the use of PCP. The drug can also produce acute behavioral toxicity consisting of intoxication, aggression, and confusion, as well as coma, convulsions, and psychoses. A PCP-induced psychosis can persist for several weeks following a single dose of the drug.

See also **Addiction: Concepts and Definitions; Epidemiology of Drug Abuse; Gamma-Aminobutyric Acid (GABA); National Survey on Drug Use and Health (NSDUH); Treatment: An Overview of Drug Abuse/Dependence.**

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DYNORPHIN. Dynorphin is a neuropeptide transmitter; it is an opioid peptide, a member of the endorphin family of peptides. All neurotransmitters like Dynorphin have receptors. Its greatest affinity is for the Kappa opioid receptor. Dynorphin's role in drug abuse was originally anticipated based on its location in anatomical areas strongly associated with the mechanism of action of drugs of abuse. It is localized in the nucleus accumbens, amygdala, and ventral tegmental area.

Dynorphin induces feelings of dysphoria, or despair. This was first documented in animals, and later confirmed in humans. It is surprising because the best known opiate-like drugs are morphine and heroin, and they present great abuse liability since they illicit feelings of euphoria and absence of pain. However, there seem to be two opioid systems controlling behavior, one influencing feelings of reward (through endorphins) and one influencing feelings of aversion (through dynorphin). The physiological substrate underlying the effects of dynorphins is believed to be at the level of the mesolimbic dopamine neurons in the ventral tegmental area. Dynorphin tonically inhibits the firing of dopamine neurons, thus preventing its release in the striatum. Elevations of dopamine levels in the

nucleus accumbens are believed to underlie the reinforcing properties of many psychostimulant-like drugs, as well as opiates.

Due to the adverse feeling associated with withdrawal from many drugs of abuse, the dynorphin system has been implicated in contributing to this state. Studies have found that there are long-term changes in dynorphin levels in brain areas associated with drug abuse, and that these changes also exist during withdrawal. Prenatal exposure to cocaine also affects the levels of dynorphin in the brain. These changes are present in both animal and human models of drug abuse. Since drugs modulate dynorphin systems, we can gain an understanding of how drugs work in the brain by studying the dynorphin system.

See also **Amygdala; Neurotransmitters; Nucleus Accumbens; Opiates/Opioids; Receptor, Drug; Ventral Tegmental Area.**

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EASTERN EUROPE. Eastern Europe is comprised of some of the countries of the former Soviet Union (Russian Federation, Ukraine, Belarus, Moldova, and the Baltic nations of Latvia, Lithuania, and Estonia) and its satellites (Poland, Romania, Bulgaria, Czech Republic, Slovakia, Hungary, Albania, and countries formed from the former Yugoslavia: Slovenia, Croatia, Serbia and Montenegro, Bosnia and Herzegovina, and Kosovo). The region is characterized by very high levels of alcohol use and, from the mid-1990s onward in the easternmost nations, by one of the highest rates of illicit injecting drug use in the world. Consequently, by the early twenty-first century, several Eastern European countries had the fastest-expanding HIV epidemics in the world, mostly among and from injecting drug users (also known as IDUs) to their sexual partners.

HISTORY OF SUBSTANCE USE

Alcohol has been used widely in Eastern Europe for several centuries. Large opium plantations existed on the Russian and Ukrainian steppes, and many Polish and Ukrainian villagers grew opium poppies near their homes as ingredients for homemade medicines to relieve pain and ease stomach ailments. The use of both cannabis and opium is believed to predate alcohol use by several millennia. The use of distilled alcohol (such as vodka) probably began in the sixteenth century, with tobacco use introduced in the early seventeenth century. Russia is also one of the leading tea-consuming nations, whereas Poland is the seventh largest consumer (in absolute terms) of coffee in the world.

Alcohol use rates in the easternmost countries of Eastern Europe are among the highest in the world. By 2007 Russia's average annual alcohol consumption had reached 15 liters per person, almost doubling the 2003 figure of 8.9 liters. For comparison, the 2003 statistics for selected other Eastern European nations were Czech Republic, 16.2 liters; Ukraine, 5.2; Belarus, 4.8; and Moldova, 10.2. In 2006, 12 billion liters of alcohol were sold in Russia, of which 75 percent was beer, 16 percent vodka and other hard liquor, 8 percent wine, and 1 percent cognac.

Although tobacco use has declined in many countries since the late twentieth century, it continues to rise in Eastern Europe. In 2004, 41.5 percent of Russians over the age of 15 smoked, compared to, for example, 21 percent of Canadians and 25 percent of Britons. Russia is the fourth largest market (in absolute terms) for tobacco in the world. The nation became an enormous market for transnational tobacco suppliers after a shortage of cigarettes in the early 1990s caused so-called tobacco riots, which led to a relaxation of import restrictions on tobacco products. A 2008 study showed that cigarette prices in Russia were low, making them widely accessible; tax on tobacco products was not keeping pace with inflation; Russia had no policies to restrict smoking in public places; Russian smokers did not have access to counseling or other support services to quit smoking; tobacco product advertising and promotion were not banned in the Russian mass media except for TV; and no functional

national tobacco control agency existed in Russia to lead tobacco control efforts.

Despite the fact that imperial Russia bordered on and interacted with opiate- and hashish-using peoples, the abuse of these substances and cocaine was relatively rare. Russian medical literature of the nineteenth and early twentieth centuries barely addressed this topic, in contrast with the plethora of works fulminating against alcoholism and tobacco smoking. Three factors discouraged the abuse of narcotics in tsarist Russia. First, alcohol was the drug of choice. Second, although British and American physicians liberally prescribed opiates in the nineteenth century, Russian medical literature and textbooks for physicians, pharmacists, and paramedics consistently warned against the indiscriminate use of opiates and cocaine. In the late 1890s, shortly after heroin entered therapeutics, Russian physicians stressed that prolonged use could lead to addiction. Physicians also presented popular lectures on the evils of drug abuse. The third factor retarding drug abuse was the nature of Russian pharmacy. Russia lacked a large pharmaceutical industry and, furthermore, the Russian government closely controlled pharmaceutical practice.

The Soviet Union long denied the existence of drug users within its borders. Whereas Soviet medical literature candidly discussed narcotic abuse in the 1920s and early 1930s, from the late 1930s to the 1950s hard data on the number of abusers were scanty. But, by 1990 the number of registered drug addicts was admitted to be approximately 300,000, including 60,000 injecting drug users. These figures were assumed to be underestimates by five to ten times. Even so, during the 1990s the number of registered drug addicts grew 16-fold in the Russian Federation. By 2004 it was estimated that 2 percent of the adult population in the federation had tried opiates (with a 1999 study showing that 6% of 15- to 16-year-olds had tried heroin); 0.8 percent in Ukraine; 0.4 percent in Belarus; and 0.1 percent in Moldova.

Illicit drug use and drug injecting in the early twenty-first century has centered on a variety of opium products and a range of stimulants. Prior to the widespread availability of heroin in the region in the mid- to late 1990s, opium was consumed in liquid preparations known variously as *hanka*, *chornye*, or poppy straw. Considerable inter- and intra-country variation existed in the ways that these liquid opiates were prepared but all were most commonly used by injection. A group of injectors would generally meet at one drug user's apartment, combine the necessary ingredients (*cook* it), prepare and inject the drug, usually drawing several times from a common cup or vial.

The advent of widespread heroin use has reduced the utilization of communal equipment for drug preparation but needle and syringe sharing has continued, leading to massive HIV epidemics among injecting drug users in Russia and Ukraine; significant epidemics in Poland, Belarus, and the Baltic countries; and smaller epidemics in Moldova, Bulgaria, and Romania. In the countries formed from the former Yugoslavia, injecting drug use has played little role so far in HIV epidemics: In these nations, the most common mode of transmission is among men who have sex with men. Similarly, little transmission has occurred among or from drug users in Czech Republic, Slovakia, Hungary, or Albania. The *2006 Report on the Global AIDS Epidemic* released by the Joint United Nations Programme on HIV/AIDS (UNAIDS) reported that 220,000 people were newly infected with HIV in Eastern Europe and Central Asia in 2005, bringing to approximately 1.5 million the number of people living with HIV—representing a 20-fold increase in less than a decade. More than 50,000 adults and children died from the disease that year. Almost all the infections were confined to two countries: Russia and Ukraine.

In addition to opioids, each country in the region appears to have some level of psychostimulant use, including injection. In Russia, a homemade product known as ephedrone or *vint* was widely used in the 1990s, but in the first decade of the twenty-first century this appears to have been replaced mostly by amphetamine and Ecstasy use. In the Czech Republic, methamphetamine or pervitin is very popular. Poland is cited in the *World Drug Report 2007* issued by the United Nations Office on Drugs and Crime (UNODC) as one of the major sources of amphetamine production in Europe. Cocaine use in Eastern Europe is very low. As well as these classes of drugs, a range of other psychoactive drugs is used illicitly. In Moscow, for example, ketamine has been injected

extensively by a subculture of street youth. In 2006 the Czech Republic was found to have the highest number of cannabis users in Europe. Czech per capita consumption of marijuana (22% of people aged 15–34 years) was about the same as that in the United States.

STATE POLICIES ON SUBSTANCE USE

Policies regulating drug and alcohol use vary widely across Eastern Europe, as do the methods available for treating drug and alcohol dependence. For licit drugs, a range of controls are in place with subtle variations from country to country. Although laws exist against under-age drinking in Russia, for example, vending machines selling cans of spirits (such as rum or gin) with mixers may be found at many Moscow Metro stations: As these are unsupervised, young people have easy access to alcohol. Alcohol use has been a major issue in Russia since at least the mid-1980s. By that time, the age at which people began to drink had fallen, increasing numbers of women and children were heavy drinkers, and in some cities the average consumption among working adults was a bottle of vodka each day. Newspapers reported that 3.5 percent of the workforce at one chemical plant were confirmed alcoholics, 2.2 percent showed early signs of addiction, and a further 18.8 percent were alcohol abusers, with only 1.4 percent abstainers. It was suggested that the loss of productivity associated with alcohol was the main reason for the Soviet Union's failure to achieve its 5-year plan in the early 1980s, with some estimates suggesting such alcohol-related loss of productivity as high as 20 percent.

The former Soviet Union was home to one of the greatest experiments in alcohol policy in the late twentieth century when the general secretary of the Communist Party, Mikhail Gorbachev, in 1985 introduced a series of measures to reduce alcohol production and sales. These included limiting the kinds of shops permitted to sell alcohol, closing many vodka distilleries and destroying vineyards in the wine-producing republics of Moldavia, Armenia, and Georgia, and banning the sale of alcohol in restaurants before two o'clock in the afternoon. (The policy lasted until 1988.) The results of this policy are still hotly debated, with some claiming a reduction in the number of cases of liver disease and other conditions several years after the ban, and others pointing to the tens of thousands of Russians who died during the late 1980s from drinking homemade *samargon* (homemade vodka) or various other nonbeverage alcohols made from products such as aftershave lotion and shoe polish. At its height, the number of poisoning deaths was estimated at 40,000 annually and, even in 2006, 28,386 alcohol-linked deaths (mostly as a result of poisoning) were reported, representing 12 percent of all deaths in Russia.

In general, the use of illicit drugs is not criminalized in most nations of the region, although their supply, sale, manufacture, and trafficking are illegal. The possession of illicit drugs for personal use has been a topic of great debate in many Eastern European countries, and laws have changed both toward heavier penalties and criminal sanctions for those found to possess small quantities of drugs, and toward greater liberalization, amounting to de facto decriminalization of the possession of illicit drugs for personal use. In some cases, such as in Russia, Poland, and Bulgaria, both changes have occurred in the space of a few years.

Dependence treatment ranges from sophisticated, evidence-based treatment systems that are beginning to reach high levels of coverage in countries such as the Czech Republic and Slovenia, to very poor treatment systems in the easternmost nations, especially in the Russian Federation, Ukraine, Belarus, and Moldova. In these countries, most drug and alcohol treatment is based on narcological theories developed during the Soviet period. Analyses of narcological methods have shown them to be generally without a solid evidence base and to be implemented often in punitive, jail-like settings. Narcology relies heavily on detoxification as a stand-alone treatment despite international evidence that detoxification alone rarely assists in stopping drug or alcohol dependency.

Virtually all the nations of Eastern Europe allow (and in some cases provide at high coverage levels) opioid substitution treatment (OST) with either methadone or buprenorphine, or both. The exception is the Russian Federation, which has passed a law specifically banning any OST using methadone and as of early 2008 still had not allowed any buprenorphine programs to be implemented. Needle-exchange programs and other programs attempting to reach injecting drug users

with HIV prevention education and materials are present in every country in Eastern Europe, although in most locations these activities are delivered at such low coverage levels that HIV epidemics continue to expand or pose the risk of rapid expansion.

See also **European Union; Foreign Policy and Drugs, United States; International Drug Supply Systems; Nordic Countries (Denmark, Finland, Iceland, Norway, and Sweden).**

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DAVE BURROWS

EATING DISORDERS.

See **Anorexia Nervosa; Bulimia Nervosa.**

ECONOMIC COSTS OF ALCOHOL AND DRUG ABUSE.

Alcohol and drug abuse continue to be major health problems in the United States in the twenty-first century. As such, they cost the nation billions of dollars in health-care costs and reduced or lost productivity each year. Since the mid-1980s, researchers have regularly estimated the direct and indirect economic costs of alcohol and drug abuse in the United States. In 1985, alcohol abuse and dependence cost an estimated 70.3 billion dollars, and in 1988 the costs had risen to an estimated 85.8 billion dollars (Rice et al., 1991).

Other estimates on the various costs of substance abuse followed in the 1990s and first decade of the twenty-first century. In 1998, the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), which are parts of the National Institutes of Health (NIH), released a study on these costs based on 1992 survey data. In 2004 the Substance Abuse and Mental Health Services Administration (SAMHSA) released a report that estimated the cost for treatment of alcohol or drug abuse in outpatient facilities, and a 2008 report by the Johns Hopkins University School of Medicine examined the high rates and rising costs of alcohol and drug disorders in hospitalized patients. A 2004 study by the Office of National Drug Control Policy (ONDCP) estimated the costs of drug abuse between 1998 and 2002.

THE EXTENT OF THE PROBLEM IN 1992

The 1998 reports by NIAAA and NIDA found that the economic cost to society from alcohol and drug abuse was $246 billion in 1992. (Alcohol abuse and alcoholism cost an estimated $148 billion, while drug abuse and dependence cost an estimated $98 billion.) Although the data in the reports is slightly dated, the analytical methods used to assess the economic costs of alcohol abuse shaped later studies of drug abuse and defined the problem for the general public.

The 1992 estimates were 42 percent higher for alcohol than the 1985 estimate, over and above increases due to population growth and inflation. Between 1985 and 1992, inflation accounted for about 37.5 percent of this increase, and population growth accounted for 7.1 percent. Over 80 percent of the increase in estimated costs of alcohol abuse was attributed to changes in data and methodology employed in the new study. This suggests that the previous study significantly underestimated the costs of alcohol abuse.

In 1992, there were an estimated 107,400 alcohol-related deaths in the United States. Many of those who died were between 20 and 40 years of age—mainly because the major causes of death, such as motor vehicle crashes and other causes of traumatic death, are concentrated among this age group. However, alcohol is also involved in numerous premature deaths among the older population because of long-term, excessive alcohol consumption. Total costs attributed to alcohol-related motor vehicle crashes were estimated to be $24.7 billion. This included $11.1 billion from premature mortality and $13.6 billion from automobile and other property destruction.

In 1992 the total estimated spending for healthcare services was $18.8 billion for alcohol problems and the medical consequences of alcohol consumption. Specialized services for the treatment of alcohol problems cost $5.6 billion. This included specialized detoxification and rehabilitation services as well as prevention, training, and research expenditures. Costs of treatment for health problems attributed to alcohol were estimated at $13.2 billion.

An estimated $67.7 billion in lost potential productivity was attributed to alcohol abuse in 1992. This accrued in the form of work not performed, including household tasks, and was measured in terms of lost earnings and household productivity. These costs were primarily borne by the alcohol abusers and by those with whom they lived. About $1 billion was for victims of fetal alcohol syndrome who had survived to adulthood and experienced mental impairment. This study did not estimate the burden of drug and alcohol problems on work sites or among employers.

The costs of crime attributed to alcohol abuse were estimated at $19.7 billion. These costs included reduced earnings due to incarceration, crime careers, and criminal victimization, as well as the costs of criminal justice and drug interdiction. Alcohol abuse is estimated to have contributed to 25 to 30 percent of violent crime.

The study estimated that 3.3 percent of social welfare beneficiaries in 1992 received benefits because of an administrative determination of drug- or alcohol-related impairment. While the 1996 federal welfare reform legislation has largely terminated alcohol or drug dependence as a primary cause for benefit eligibility, these impairments resulted in transfers of $10.4 billion in 1992, with administrative and other direct service expenses put at $683 million for those with alcohol problems.

A large amount of the economic burden of alcohol abuse falls on the part of the population that does not abuse alcohol. Governments bore costs of $57.2 billion (38.6 percent of the total) in 1992, compared with $15.1 billion for private insurance, $9 billion for victims, and $66.8 billion for alcohol abusers and members of their households. These costs are imposed on society in a variety of ways, including alcohol-related crimes and trauma (e.g., motor vehicle crashes); government services, such as criminal justice and highway safety; and various social insurance mechanisms, such as private and public health insurance, life insurance, tax payments, pensions, and social welfare insurance.

LATER STUDIES

The 2004 SAMHSA report found that in 2002 it cost an estimated $1,433 for each course of alcohol or drug treatment, while residential treatment cost $3,840 per admission. Outpatient methadone treatment was the most expensive, costing $7,415 per admission in 2002.

The 2008 report by researchers at Johns Hopkins found a high prevalence of hospital admissions for people who were abusing alcohol and drugs (Santora et al., 2008). The 43,000 patients admitted to Johns Hopkins between 1994 and 2002 who were abusing alcohol and drugs accounted for 13.7 percent of all hospital admissions during that time. Overall hospital costs for these patients, adjusted for inflation, increased 134 percent during the 12-year period. Medicaid and Medicare patients accounted for 70 percent of the patients and 70 percent of the costs. In 2002 the cost of caring for these patients was $28 million.

The 2004 study by the ONDCP estimated the economic costs of drug abuse in 2002 to be $180.0 billion. This amount represents both the use of resources to deal with health and crime consequences as well as the loss of potential productivity from disability, death, and withdrawal from the workforce. The study found the costs of drug abuse had increased an average of 5.3 percent a year from 1992 to 2002. This rate was slightly above the 5.1 percent annual growth in the U.S. gross domestic

product during this period. Health-care costs accounted for $16 billion of the 2002 amount, while loss of productivity accounted for $128.6 billion. The greatest share of productivity loss was from criminal activities, which included the costs of incarcerating 660,000 offenders who committed crimes to support their drug use. Police protection, federal drug control efforts, and the operation of state and federal prisons were the other major cost components, totaling 36.4 billion in 2002.

The ONDCP study also confirmed that drug abuse is one of the most costly health problems in the United States. These costs are comparable to those for other health issues, including heart disease, cancer, diabetes, Alzheimer's disease, stroke, smoking, obesity, alcohol abuse, and mental illness. Alcohol and drug abuse are costly to the United States in terms of resources used for care and treatment of persons suffering from these disorders, lives lost prematurely, and reduced productivity. Data show clearly that the measurable economic costs of alcohol and drug abuse continue to be high.

See also **Accidents and Injuries from Alcohol; Accidents and Injuries from Drugs; Aging, Drugs, and Alcohol; Alcohol and AIDS; Cancer, Drugs, and Alcohol; Complications: Medical and Behavioral Toxicity Overview; Complications: Cardiovascular System (Alcohol and Cocaine); Complications: Cognition; Complications: Endocrine and Reproductive Systems; Complications: Immunologic; Complications: Liver (Clinical); Complications: Mental Disorders; Complications: Neurological; Complications: Nutritional; Complications: Route of Administration; Crime and Alcohol; Crime and Drugs; Driving, Alcohol, and Drugs; Drug Interactions and Alcohol; Productivity: Effects of Alcohol on; Social Costs of Alcohol and Drug Abuse.**

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ED50. The ED50 is the median effective dose—the dose of a drug that is required to produce a specific effect (e.g., relief from headache) in 50 percent of a given population. The ED50 can be estimated from a dose-effect curve, where the dose of the drug is plotted against the percentage of a population in which the drug produces the specified effect. Therefore, if the ED50s for two drugs in producing a specified amount of relief from headache are 5 and 500 milligrams, respectively, then the first drug can be said to be 100 times more potent than the second for the treatment of headaches.

See also **LD50.**

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EDUCATION AND PREVENTION. *See* **Prevention, Education and.**

EMPLOYEE ASSISTANCE PROGRAMS (EAPS). An Employee Assistance Program (EAP) consists of employer-sponsored services intended to aid employees with personal problems that may adversely affect their job performance. Initially developed to address alcohol-related problems, over the last fifteen years EAPs have emerged as a common response to the problems of alcohol and drug abuse in the workplace. In addition, they provide a variety of services to help employees and their families resolve health, emotional, marital, family, financial, or legal concerns.

While the exact mix of services provided depends on a number of variables, such as size and type of company, EAPs generally offer, at a minimum, confidential client counseling, problem assessment, and treatment referral. A comprehensive EAP offers

1. assessment and referral—EAPs conduct psychosocial assessments to guide decisions to refer clients to treatment and the choice among treatment alternatives
2. treatment follow-up—client follow-up and reintegration into the workplace is an essential EAP function
3. supervisor, management, and union representative training—training provides the information needed on how and when to use the program and how to best assist employees who use it
4. employee education—information on a broad range of problems and how to use the EAP.

The delivery of EAP services may take several forms, depending on such factors as the organization's size and structure. Large companies and organizations, unions, and employee groups often operate their own programs. These services are most often housed within the human resources or medical departments. Smaller organizations, or organizations with dispersed worksites may find it more advantageous to contract with an independent EAP provider located outside the company. A newer trend among small employers is the development of consortium EAP arrangements in which a number of small employers contract with an external provider to provide EAP services.

In the past 30 years, the number of EAPs has grown dramatically. A 2008 National Study of Employers found that the percentage of employers providing EAPs rose to 65 percent in 2008 from 56 percent in 1998. The Department of Labor's Bureau of Labor Statistics found that of those employers sampled the probability of an establishment offering EAP services increased as a function of establishment size, ranging from 79 percent of employers with over 250 employees, to 9 percent of employers with fewer than 50 employees.

Rapid growth in the number of EAP programs has led to heightened scrutiny concerning their cost effectiveness; in the current economic climate, EAP programs will experience increased pressure to conduct evaluation studies that provide empirical evidence of their efficacy. More research is needed to identify and improve the most essential program components and to aid in tailoring programs to fit specific needs.

Costs incurred in providing EAP services vary widely, but their presence has been clearly tied to overall savings in a number of areas. As of 2000, the Employee Assistance Program Association found that EAPs reduce lost time by 30 percent, reduce accident and sick pay by 60 percent, and reduce accidents by 70 percent.

For many companies, the approach taken to minimize the impact of drugs in the workplace incorporates a number of additional elements that complement EAPs and constitute a comprehensive strategy. These include a clearly stated formal policy

prohibiting drug use, consequences for violating the policy, and alternative strategies to deter drug use.

The Employee Assistance Professionals Association may be consulted for further information: Suite 1001, 4601 North Fairfax Drive, Arlington, VA 22203, http://www.eapassn.org.

See also **Drug Testing Methods and Clinical Interpretations of Test Results; Industry and Workplace, Drug Use in; Military, Drug and Alcohol Abuse in the United States; Productivity: Effects of Alcohol on; Productivity: Effects of Drugs on.**

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ENDORPHINS. Endorphins are a group of peptides with potent analgesic properties that occur naturally in the brain. The word *endorphin* is a contraction for the words *end*ogenous and *morphine*; it was coined by narcotics researchers in 1975 as the preferred term for a then hypothetical natural substance capable of action at receptors for opiates (such as heroin). The underlying hypothesis was that an endorphin neurotransmitter utilized the receptors at which morphine and related drugs exerted their actions. After extensive and intensely competitive research by many groups, three distinct types of such endogenous opioid peptides were found (*peptides* are segments of linked amino acids that can act as neurotransmitters). By 2008, additional peptides able to act at opioid receptors as well as to regulate pain sensitivity through nonopioid receptors had been identified.

Each type of opioid peptide gives rise to one or more opioid peptide prohormones, which are then modified by enzymes in tissues to convert the larger inactive peptides into smaller active ones. For example, the pro-opiomelanocortin prohormone is synthesized in the corticotropes in the anterior pituitary gland and separately in hypothalmic and medullary neurons. It is cleaved in those cells to β- endorphin, a 31 amino-acid peptide with the greatest intrinsic opioid activity. Each active natural opioid peptide contains the tetrapeptide tyrosine-glycineglycine-phenylalanine at its amino terminus. The fifth amino acid is either methionine (resulting in the so-called Met^5 enkephalin) or leucine (resulting in leu-enkephalin). Opioid peptides derived from plants—for example, caseimorphin—have also been described. The opioid peptides, of which the proenkephalin- and prodynorphin-derived peptides are most widespread, are found in specific neurons in the brain.

See also **Enkephalin; Opiates/Opioids.**

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FLOYD BLOOM

ENKEPHALIN. Enkephalin is either of two pentapeptides (containing five amino acids) with opiate and analgesic (painkilling) activity, occurring naturally in the brain, with a marked affinity for opiate receptors. Endorphin was initially the name for all opioid-like neurotransmitters in the brain; the research team of Hans Kosterlitz and John Hughes gave their own name, enkephalin (a variant of *en-cephal* ["of the brain"]), to the two opioid pentapeptides that they had purified from ox brains (ca. 1977). They confirmed their discovery by showing that the effects of synthetic peptides were the same in bioassays using opiate receptors and that both Met5enkephalin and Leu_5enkephalin were authentic endogenous opioid peptides.

See also **Opiates/Opioids.**

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FLOYD BLOOM

EPIDEMICS OF DRUG ABUSE IN THE UNITED STATES.

James Anthony defined an epidemic as

> an unusual occurrence of an infection, disease, or other health hazard in a population. . . . If the number of cases occurring in the population this month (or year) is notably greater than the number of cases that occurred in the population during each of the prior months (or years), then it is legitimate to talk of a growing epidemic. (2001, p. 487)

Epidemics of substance use may look very different depending on whether they are analyzed by substance type (tobacco, alcohol, cocaine, heroin, etc.), by geographic area, by demographic group, or by some criterion other than a national overview. A nationwide look at prevalence rates of marijuana or cocaine consumption may present a picture that does not reflect trends among, for example, inner city minority populations, or people of a specific age group, or residents of a particular city. The focus of this article is one of social history; it regards drug epidemics as large-scale cultural phenomena that reflect shifts in values or perspectives among significant portions of the population. Readers may wish to consult the entry on Epidemiology of Drug Abuse for a detailed look at how epidemiologists study national drug trends and some results from recent surveys of drug use and abuse.

A fundamental question in studying the social and cultural significance of substance-use epidemics over time is how to know what drives increases and decreases in overall consumption. Why is it that some types of drugs like heroin and cocaine appear to be repeatedly involved in successive epidemics? Social demographer K. Singh reasoned that, as the number of people aged 15 to 25 in the population declined, this by itself would change the balance of susceptibility to drug use (Anthony, 2001). Thus an epidemic in the use of a drug most attractive to youth would decline over time simply because their number in the population decreased. The underlying etiology may be that a susceptible age cohort (study group) is most likely to experiment with a substance from a prior epidemic that is perceived to be safe because memories of its effects disappear from society or are disregarded as antiquated. This group of new users then becomes the foundation population for a repeat epidemic that evolves over time until the age group learns from its own experience what previous generations had also learned, or simply outgrows the desire to use drugs (ages out). To be sure, this decline is not a specific event, and some portions of the population form the vanguard while others lag behind.

Lana Harrison, citing Eric Wish, pointed out that drug use patterns and trends among arrestees may be very different from those observed in the general population. Given the general picture of deviance among arrestees, it is possible to conclude that they use illegal drugs first as the substances become available, but realize the harms of drug use later than members of mainstream society and are more likely to resist pressures to abstain (Harrison, 1992). For these reasons, certain drugs may persist in more deviant groups even after they have been abandoned by the general population.

Significantly, the U.S. Census Bureau reported that the percentage of the population in the age group most susceptible to drug use, youths ages 15 to 25, hovered just under 20 percent from 1900 to 1910—the highest percentage of the twentieth century and coincident with high rates of alcohol and drug use. This age group rose from a low of about 13 percent to just over 19 percent between 1955 and 1975 and began another precipitous decline in 1980, again coinciding to some extent with falling levels of substance use. (Baby boomers were in their teens in the early 1960s, when marijuana became popular. They reached their 30s in the 1980s as drugs in general, and particularly cocaine, began to be seen as dangerous and undesirable.)

Although there were many attempts to estimate the number of addicts in the United States beginning in the 1920s, it was not until the early 1970s that the federal government supported

systematic surveys to gauge the extent of the problem. The National Household Survey of Drug Abuse, now called the National Survey on Drug Abuse and Health (NSDAH), the Drug Abuse Warning Network (DAWN), the Monitoring the Future Survey, and Arrestee Drug Abuse Monitoring Program (ADAM) are discussed in separate entries in this work.

U.S. DRUG EPIDEMICS

What appear to be successive *waves* or cycles of substance use, followed by periods of reform have been studied by a number of scholars, particularly David F. Musto, David Courtwright, and Ruth Engs. Following is a chronological outline of these periods and a discussion of trends in acceptance and rejection of substances.

1865–1920—The First Epidemic. With the exception of the extremely high levels of alcohol use in colonial America and the early republic (Rorabaugh, 1979), the first epidemic of psychoactive substance abuse in the United States occurred in the second half of the nineteenth century and reached a peak in the first decade of the twentieth (when, as noted, the proportion of young people in the population was very high). Civil War veterans had become habituated to morphine through medical treatment, and large numbers of middle class women became addicted to opiate-based substances, either through doctors' prescriptions or self-medication with unregulated patent medicines.

The German pharmaceutical company Bayer introduced heroin in 1898 as a cough remedy, and it quickly became the drug of choice among young male slum dwellers and petty criminals. Opium dens in larger cities were frequented by prostitutes, pimps, and other marginal types as well as thrill-seeking socialites. Soft drinks and enhanced wines contained coca, and refined cocaine hydrochloride was available on the black market and in over-the-counter products such as inhalers for nasal congestion. David Courtwright reported that more than half the prostitutes in the Fort Worth, Texas, jail in 1900 were cocaine addicts.

Per capita ethanol consumption in the United States among people over the age of 14 ranged from a high of 2.6 gallons a year between 1906 and 1910 to 1.96 gallons just before National Prohibition was enacted in 1920. (By way of comparison, the years between 1935 and 1944 showed consumption well below two gallons, and below one gallon in 1934) (National Center for Health Statistics, 2006).

The excesses of the age inspired passionate reformist sentiments that found expression in temperance movements and drives for government regulation of food and medicine. These campaigns were instrumental in securing passage of federal legislation controlling commerce and consumption of psychoactive substances: the Pure Food and Drug Act of 1906, the Opium Exclusion Act of 1909, the Harrison Anti-Narcotics Act of 1914, and last but not least, the Nineteenth Amendment to the Constitution prohibiting "manufacture, sale, or transportation of intoxicating liquors," which became law in 1920.

1920–1960. Early in the twentieth century, about the same time that the International Opium Convention, the first international treaty on drug control, was signed at The Hague (January 23, 1912), the United States experienced an increase in tobacco smoking, with peak population levels of smokers occurring during World War II and the following two decades.

When one considers the social climate of the early twenty-first century, a time when tobacco smoking is not a socially approved drug-use practice, it may be difficult to imagine that, during World War II, Lucky Strikes and other cigarettes were passed out to soldiers as part of their daily food rations. This turned out to be an effective way to sustain the epidemic of tobacco smoking, but one cannot be sure whether the tobacco industry's intent was primarily to boost the morale of soldiers or to create and build market strength for tobacco cigarettes (Anthony, 2001)

From 1920 through the early 1960s, cocaine, heroin, and marijuana use in the United States was unusual outside of relatively small circles of entertainment stars, jazz musicians, and others who came into contact with illicit suppliers of drugs. The Marihuana Tax Act of 1937 succeeded in placating popular fears of the corrupting influence of alien minorities (mostly supposed to be Mexican) rather than responding to a documented increase

in use. The Act served both to address a perceived threat and to demonstrate that H. J. Anslinger's Federal Bureau of Narcotics had the situation under control (Musto, 1987).

Alcohol use began a slow rise after repeal of Prohibition but did not reach new highs until 1970. In the early 1970s, when the federal government began supporting a series of national and state surveys of illicit drug use, cocaine use was found so rarely that it was difficult to get a reliable impression of the characteristics of the cocaine users—there were too few of them in the national survey samples. This was a period of low levels of drug use in all sectors of society and of enthusiasm for harsh penalties for drug trafficking and possession (the Boggs Act of 1951 and the Boggs-Daniels Act of 1956).

Retrospective data analyzed in the National Survey on Drug Abuse in 1977 indicated that lifetime experience with any illicit drug did not exceed 2 percent of the general population in the early 1960s. Marijuana use among young males and some ethnic minorities was estimated at approximately 5 percent. Then the spirit of the times changed. The reason may have been demographic, economic, political, or some combination of these forces, but the result was a period of extreme social stress in the United States.

1960–1980—The Second Epidemic. In the late 1960s and early 1970s, the middle class enjoyed unparalleled economic prosperity that permitted its sons and daughters long periods of intellectual and leisure activity. These young people, who as noted were becoming an ever-larger proportion of the population, adopted political positions and lifestyles at odds with the values of the preceding generation. In large numbers they took up the causes of civil rights, opposition to the war in Vietnam, and—what they saw as their right—use of mood-altering substances of various kinds. Thus, a process analogous to the large-scale violation of alcohol prohibition laws was set in motion: As a proscribed activity is adopted by some members of the middle class, the laws that apply to that behavior are increasingly questioned. The National Commission on Marijuana and Drug Abuse reported in 1972 that 83 percent of the adults surveyed and 65 percent of the youth would not incarcerate a youthful first offender; 54 percent of the adults and 41 percent of the youth were opposed to imposing a police record on young offenders. By this time, drug policymaking reflected both the scientific and popular opinion that treatment should be the focus of drug policy, that severe penalties were counterproductive, and that abuse was a product of environment and could be controlled by manipulation of the external circumstances of the user. In spite of President Richard M. Nixon's declaration of "war on drugs" in 1971, his administration saw a large increase in budget allocations for treatment programs and the first large-scale implementation of methadone maintenance for heroin addicts. As part of this effort, the president established the Special Action Office for Drug Abuse Prevention (SAODAP) with Jerome Jaffe as its head.

In part, these policies were motivated by the return of Vietnam veterans, many of whom had become users of heroin and other opioid drugs during their overseas tours of duty. This surge in heroin use in the late 1960s and early 1970s was documented most readily by examining statistics on clients entering treatment for heroin dependence, including the lag of several years that separated users' initial injection of heroin to their first admission for treatment. Despite the war on drugs, another smaller increase in heroin use or dependence occurred during the mid-1970s, followed by apparent decreases in the occurrence of heroin dependence during the late 1970s and early 1980s. The early decrease appears to have coincided with the decrease in importation of heroin to the United States from supplier countries such as Turkey, and the mid-1970s increase with the emergence of Mexico and Southeast Asia as suppliers of illicit opiates.

The only drug-taking behavior that decreased during this period was tobacco smoking. The 1962 Surgeon Generals Report on Smoking and Health added new urgency to publicity campaigns about the health hazards of smoking. Per capita cigarette consumption did not decline significantly until the late 1970s, when that figure stood at under 4,000 cigarettes per year according to the American Lung Association (2004). After that, the number decreased steadily. While it is difficult to determine if social opprobrium was the primary factor in this trend, it is certainly true that smoking has become

socially unacceptable among large segments of the population, and controlling legislation is popular in spite of protests from civil libertarians. It is ironic that a trend toward strict regulation of tobacco smoking began as efforts to decriminalize marijuana were gathering support.

Alcohol consumption also rose during this period to exceed levels registered at the beginning of the twentieth century. A high of 2.76 gallons per capita was recorded for 1980 and 1981. After that, consumption rates declined until 1998, when levels were reported at 2.14 gallons. Rates have increased somewhat since then (National Center for Health Statistics, 2006).

1980–1990. During the last years of the administration of President Jimmy Carter (1977–1981), parents of young teenagers complained that government leaders were promoting an attitude of accommodation to recreational drugs that was contributing to widespread use among their children. Carter endorsed decriminalization of marijuana in 1976, and his health adviser and drug czar was widely quoted as believing that cocaine was relatively benign. But rejection of these positions gradually took hold, at least among middle-class citizens. The period from 1978 to 1985 may be seen as a transition during which people in favor of moralistic and legalistic approaches to drug control struggled to gain political leverage, first over marijuana use among their own rebellious children, and later against the image of cocaine as the glamorous high of the media celebrity or hot-shot businessperson.

There may be a parallel between the story of cocaine and that of heroin. Heroin, the effects of which were initially hailed after it was first produced in 1898, later proved so devastating that by 1924 it was entirely rejected by the medical establishment, new manufacture was outlawed by Congress, and it became emblematic of degradation and marginalization. It never really emerged from this literal and figurative ghettoization. When it did appear among middle-class youth in the 1970s, it caused generalized consternation, and middle-class use, while an epidemic in the sense of an unusual and measurable increase, was relatively limited. In 1972 the National Household Survey on Drug Abuse reported that the rate of lifetime heroin use among young adults was 4.6 percent with current use below measurable levels. Mainstream society had not forgotten that heroin was a dangerous and frightening drug—all the more so for its association with suspect urban subcultures and a mode of administration, intravenous injection, not likely to appeal to casual experimenters.

In the case of cocaine, it had been possible for middle-class drug users to forget or ignore the lessons that medical practitioners, social activists, and drug users themselves had learned between the late nineteenth century and the 1920s. Unlike heroin, cocaine had not remained a presence at the margins of middle-class experience and, when it emerged in the early 1970s, it seemed entirely new. Current (past month) use among young adults reached 9.3 percent in 1979. But as attitudes changed and experience grew, rates began a slow decline. Current use was down to 6.8 percent in 1982, 7.6 percent in 1985, and 4.5 percent in 1988. In the late 1980s, as middle-class cocaine use was already on the wane, crack, a new smokeable form of cocaine, appeared and quickly became a feature of life in urban areas populated by the minority poor, thereby effectively relegating cocaine to the list of "bad" drugs along with heroin.

While self-report surveys of the general population were showing declines in cocaine use, a new program, the Drug Use Forecasting program (DUF, now called ADAM) was showing a growing problem among arrestees. Urine tests obtained from samples of arrestees in booking facilities across the United States showed that 80 percent or more of arrestees, regardless of charge, tested positive for cocaine as well as other drugs. These findings alerted the nation to the extreme drug problems in offenders and led to new treatment and drug court programs to address this population. Even by the early twenty-first century, when levels of cocaine use declined markedly in the general population as the crack epidemic waned, a sizable minority of arrestees in the largest cities of the country still tested positive for cocaine and other illegal drugs.

A somewhat odd drug-taking fashion appeared between the mid-1980s and the early 1990s, mostly among adolescent males—smokeless tobacco (Nelson et al., 2006). This phenomenon has been traced to deliberate marketing strategies, including formulation of relatively low-cost, "unit dose"

supplies of tobacco snuff that were flavored to increase palatability (Anthony, 2001).

The major drug surveys measure changing perceptions of the dangers of given substances among the selected responding populations, and increases in perception of risk are correlated to declines in use. Some specific events have been tied to increases in perceptions of risk, but other factors make the social environment more or less receptive to the lessons of these events. The drug-related deaths of Jimi Hendrix and Janis Joplin in the fall of 1970 had little impact on attitudes toward drug taking, while those of Don Rogers and Len Bias from the effects of cocaine in 1986 elicited a public response.

1991 to the Early Twenty-first Century. By the mid-1990s, multiple indications showed that the nation was in the end-stages of its second major drug epidemic. The peak years of the epidemic seem to have been in the early-to-mid-1980s. Past-month cocaine use in the general population over 12 years of age stayed below 1 percent throughout the decade of the 1990s, according to the National Household Survey on Drug Abuse (now called the National Survey on Drug Use and Health). That measure increased to one percent in 2003, decreased to 0.8 percent in 2004, and returned to one percent again in 2005 and 2006. The Monitoring the Future Survey reported past-month cocaine use among young adults aged 19 to 28 below two percent from 1992 through 2000, then a slight up-tick to 2.4 percent in 2003. Trends in annual prevalence in use of any illicit drug other than marijuana among all age groups reported in this survey show a peak in 1981 and relative stability after 1993, with some increases among young adults between the ages of 19 and 24. (People aged 21 to 22 reported an annual use rate of 22 percent in 2006—higher than the 13.5 percent recorded in 1993 but well below the 1981 level of 37 percent.)

With respect to smoking, the American Lung Association reports that adults consumed fewer than 2,000 cigarettes per capita in 2003. The percentage of American adults who were current smokers had declined to 22.5 percent in 2002, again according to the American Lung Association. The National Survey on Drug Use and Health puts the 2002 figure at 26 percent and 25 percent in 2006. The smokeless tobacco vogue, principally among adolescent males, had plummeted by nearly 50 percent by 2006 (Nelson et al., 2006).

As the use of cocaine and heroin declined in the general populations, other drugs took their place. Methamphetamine abuse has been reported in many states, especially in the west and southwestern parts of the United States. Spikes in use have been found from time to time in MDMA (Ecstasy) and marijuana by youths and in the misuse of prescription drugs. Stimulants are being shared by ADHD patients with their college peers. Increases in the use of prescription analgesics, including methadone, buprenorphine, and oxycodone, are showing up in surveys and in death statistics from medical examiners. The history of drug epidemics is consistent with the view that peoples' appetites for psychoactive drugs persist, while perceptions of risk and rates of use vary, and that the specific drugs of abuse change over time with each new generation.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Arrestee Drug Abuse Monitoring (ADAM and ADAM II); Cocaine; Cola/Cola Drinks; Drug Abuse Warning Network (DAWN); Epidemiology of Drug Abuse; Harrison Narcotics Act of 1914; Heroin; International Control Policies; International Drug Supply Systems; Marijuana (Cannabis); MDMA; Methadone Maintenance Programs; Methamphetamine; Mexico; Monitoring the Future; Morphine; National Survey on Drug Use and Health (NSDUH); Opiates/Opioids; Oxycodone; Parent Movement, The; Prescription Drug Abuse; Prohibition of Alcohol; Psychoactive; Temperance Movement; Tobacco: Smokeless; U.S. Government Agencies: Special Action Office for Drug Abuse Prevention (SAODAP); Vietnam War: Drug Use in U.S. Military.**

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ERIC WISH

EPIDEMIOLOGY OF ALCOHOL USE DISORDERS.

Epidemiology is the study of the distribution and determinants of health outcomes in a population. *Distribution* refers to the incidence and prevalence of health outcomes in the population as a whole or within subgroups of the population, as well as to trends over time in health outcomes. *Determinants* are factors that predict an increased risk for the onset or persistence of health outcomes. Unlike other branches of medicine, epidemiology focuses on factors affecting disease in a particular population or larger community. A "population of interest" may be a group defined by age, sex, or race and ethnicity, or it may be groups of patients in treatment facilities. A "community of interest" may comprise household residents in a particular geographic area.

Of concern here is the epidemiology of alcohol abuse and dependence (referred to together as "alcohol use disorders"). The definition of alcohol use disorders used throughout will refer to the *DSM-IV* definitions of the disorders. First, information on historical trends in alcohol consumption will be reviewed. As alcohol consumption is a necessary, but not sufficient, cause of alcohol abuse and dependence, the study of alcohol consumption can provide clues about trends in abuse and dependence in time periods for which diagnostic information is unavailable. Second, the design and results of major U.S. surveys in which the prevalence of alcohol abuse and dependence has been estimated will be analyzed. Third, the course of alcohol disorders will be examined by looking at onset, duration, recovery, and treatment rates. Finally, there will be an overview of major risk factors for alcohol abuse and dependence.

HISTORICAL TRENDS IN ALCOHOL CONSUMPTION

Long-term historical information on U.S. alcohol consumption is available through per capita alcohol consumption statistics derived from sales figures. These statistics do not reflect the prevalence of

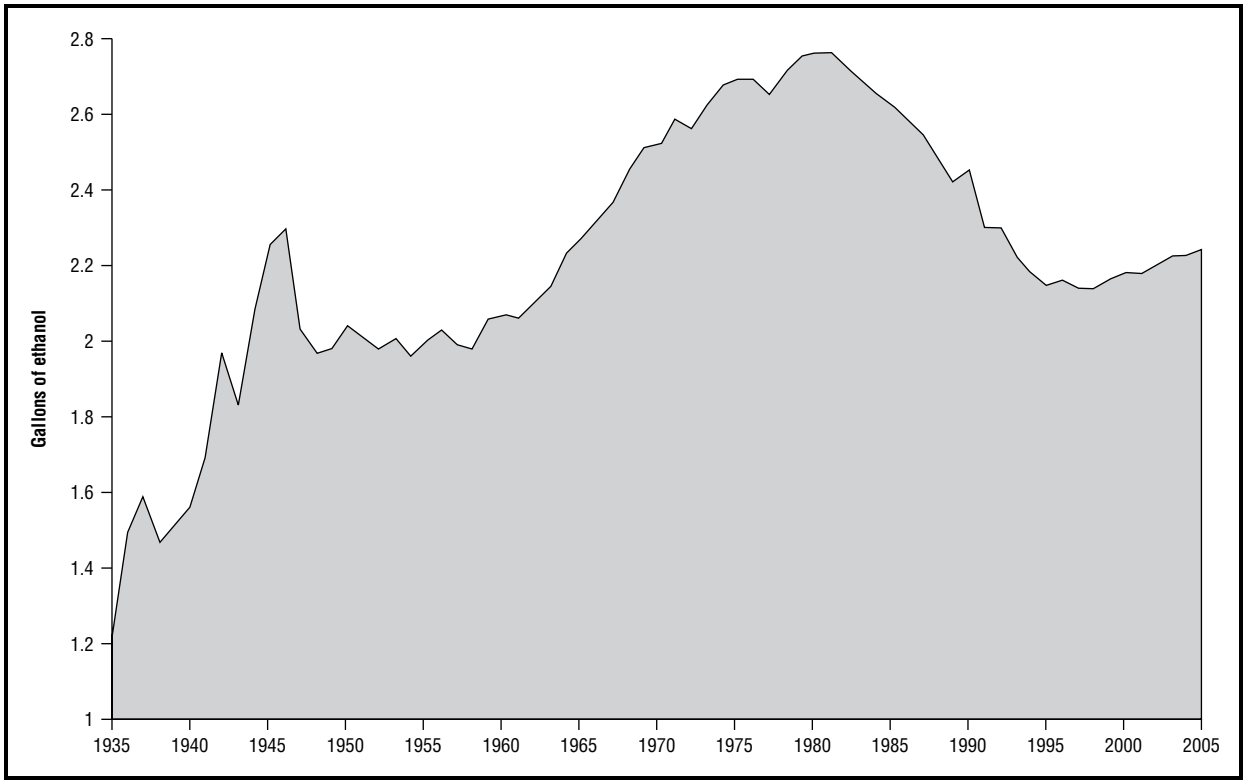

Figure 1. Total per capita ethanol consumption, United States, 1935–2005. (Source: Lakins et al., 2007.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

alcohol use disorders, but the statistics do provide information from the 1700s to the present on alcohol consumption, a necessary condition for the development of alcohol dependence or abuse. However, these statistics only reflect alcohol sales, not the totality of alcohol consumption (especially during the period of Prohibition). Despite this limitation, studies of long-term trends in alcohol sales provide a historical picture of alcohol consumption in the United States, and this can give valuable clues regarding trends in alcohol abuse and dependence before specific diagnostic criteria were established.

These figures show drinking levels in the U.S. varied greatly over time (Lender & Martin, 1982). Per capita consumption levels ranged from extraordinarily high levels during the U.S. colonial period (from an estimated 5.8 gallons per year per capita in 1790 to 7.1 gallons in 1830) to very low levels before and during Prohibition, which began in 1919 (from an estimated 1.96 gallons in 1916 to 0.97 gallons in 1934). Levels were high during the colonial era because water supplies were unsafe, so that even children drank alcohol. Figure 1 shows the estimated per capita alcohol consumption from the end of Prohibition in 1933 through 2005. From 1935 until 1982, per capita alcohol consumption increased steadily to a peak of nearly 2.8 gallons of ethanol per year in 1982 (Lakins et al., 2007). Since then, consumption has declined, leveling off at about 2.2 gallons of ethanol per year in 1993, and remaining at around that level until 2005, with a slight increase from 1999 to 2005. These data are generally consistent with liver cirrhosis mortality statistics, which show similar variations over time (Yoon et al., 2006).

Surveys are another source of alcohol consumption information. These surveys ask a representative sample of individuals to self-report on alcohol consumption. The advantage of surveys over alcohol sales data is that subgroup variations in alcohol consumption can be examined. The main disadvantages are that yearly information is often not available and individuals can underreport their alcohol consumption. Several national alcohol surveys have focused on direct questions about

Feature	ECA	NCS	NLAES	NCS-R	NESARC
Sponsoring institution	NIMH	NIMH	NIAAA	WHO	NIAAA
Years of data collection	1980–1984	1990–1992	1991–1992	2001–2003	2001–2002
Sample size	20,219	8,098	42,862	9,282	43,098
Response rate (approximate)	77.60%	82.60%	89.20%	70.90%	81.00%
Sample	5 U.S. communities	U.S. general population	U.S. general population	U.S. general population	U.S. general population
Sampling method	Probability, block sampling and oversampling in some sites	Probability	Probability, oversampling for minorities and young adults	Probability	Probability, oversampling for minorities and young adults
Individuals surveyed	Household+ institutional residents	Household and college residents	Household residents	Household and college residents	Household and group quarters residents
Age range	18 and older	15–54	18 and older	18 and older	18 and older
Field work conducted by:	Independent academic researchers at the five sites	Survey Research Institute, University of Michigan	U.S. Bureau of the Census	Survey Research Institute, University of Michigan	U.S. Bureau of the Census
Follow-up component	1-year follow-up at all sites (N=10,167), ongoing 13-year follow-up at the Baltimore site	10-year follow-up (N=4,375)	None	None	1-year follow-up, N=34,653

Table 1. Design features of the five U.S. third-generation psychiatric epidemiological studies. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

consumption and nondiagnostic scales of alcohol-related problems. Conjoint analysis of several of these surveys showed that the lifetime and current prevalence of multiple alcohol-related problems increased in the U.S. general population from 1967 to 1984 (Hasin et al., 1990), but decreased from 1985 to 1995 (Greenfield et al., 2000; Hilton, 1987). The consistency of these findings lends credence to both sales-based and survey data.

PSYCHIATRIC EPIDEMIOLOGIC SURVEYS: AN OVERVIEW

Unlike alcohol consumption, which in itself is not a disorder, alcohol abuse and dependence are specific diagnoses defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*). The *DSM-IV* stipulates that individuals must exhibit a maladaptive pattern of alcohol consumption accompanied by specific criteria. Most available information on the prevalence of alcohol use disorders in the general U.S. population comes from large-scale psychiatric epidemiologic surveys conducted after the 1970s. Prior to the 1970s, large-scale epidemiologic studies did not address alcohol use disorders and generally used a very different methodology. In the mid- and late-1970s, diagnostic methods in psychiatry changed, allowing the use of specific diagnostic criteria for disorders including alcohol use disorders (Spitzer et al., 1978). This advance in methodology led to five major large-scale psychiatric epidemiologic studies based on specific diagnostic criteria: the Epidemiologic Catchment Area Survey (ECA), the National Comorbidity Survey (NCS), the National Longitudinal Alcohol Epidemiological Survey (NLAES), the National Comorbidity Study Replication (NCS-R), and the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Table 1 shows numerous features of each study.

PSYCHIATRIC EPIDEMIOLOGIC SURVEYS: DESCRIPTIONS OF EACH STUDY

In these surveys, large sample sizes and a wide geographic distribution of data collection has precluded the use of clinicians as interviewers. Therefore, structured diagnostic interviews were developed that could be administered by nonclinicians to collect data on symptoms and criteria of psychiatric disorders, including alcohol use disorders. Table 2 shows the diagnostic assessment procedures used in the five studies. Each interview form has distinctive structural features, and some, such as the NCS-R, appear to have influenced the rates of alcohol dependence obtained.

Epidemiologic Catchment Area Study (ECA).

The ECA, the earliest of the three major third-generation studies, was conducted between 1980

Feature	ECA	NCS	NLAES	NCS-R	NESARC
Diagnostic criteria used	DSM-III	DSM-III-R	DSM-IV	DSM-IV	DSM-IV
Diagnostic interview	Diagnostic Interview Schedule (DIS)	Composite International Diagnostic Interview - U. Michigan version (UM-CIDI)	Alcohol Use Disorders and Associated Disabilities Interview Schedule (AUDADIS)	Composite International Diagnostic Interview - WMH (WMH-CIDI)	Alcohol Use Disorders and Associated Disabilities Interview Schedule-IV (AUDADIS-IV)
Psychometric testing of interview	Comparison to other diagnostic procedures in varied settings indicated good reliability for alcohol diagnoses	None for this version of the CIDI	Test-retest reliability in three samples; kappas ranged from 0.70 to 0.84 for alcohol diagnoses	Clinical reinterviews with the Structured Clincial Interview for DSM-IV low sensitivity and excellent specificity for alcohol diagnoses	Test-retest reliability in two general population samples; kappas ranged from 0.70 to 0.74 for alcohol diagnoses
Time frame for "current" alcohol use disorder	Prior six months	Prior six months	Prior 12 months	Prior 12 months	Prior 12 months
Diagnostic coverage	Substance use, affective, anxiety, psychotic disorders	Substance use, affective, anxiety, psychotic disorders	Substance and unipolar affective disorders	Substance, affective, anxiety, psychotic disorders	Substance use, affective, anxiety, personality disorders, psychotic screening
Notable interview features	Probe flowchart eliminates psychiatric symptoms if subject attributes them to alcohol/drugs	Screening questions all at start of interview, subject's commitment to disclosure requested then	Past alcohol disorders not diagnosed unless symptoms clustered together syndromally as specified in DSM-III-R and DSM-IV, alcohol abuse and dependence assessed hierarchically* and non-hierarchically	Screening questions all at start of interview, subject's commitment to disclosure requested then. In a departure from DSM-IV guidelines, alcohol dependence only assessed among individuals meeting criteria for alcohol abuse.	Past alcohol disorders not diagnosed unless symptoms clustered together syndromally as specified in DSM-III-R and DSM-IV, alcohol abuse and dependence assessed hierarchically* and non-hierarchically

*The DSM-IV specifies a hierarchical relationship between alcohol abuse and dependence. Individuals who meet lifetime criteria for alcohol dependence cannot be diagnosed with alcohol abuse. The NLAES interview collected information on alcohol abuse and dependence for all respondents regardless of alcohol dependence status so that diagnosis prevalence could be reported hierarchically or non-hierarchically.

Table 2. Assessment features of the five U.S. third-generation psychiatric epidemiologic studies. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

and 1984. One explicit purpose of this study was the assessment of psychiatric disorders according to the then-new *DSM-III* nomenclature. Unlike the remaining surveys discussed below, the ECA surveyed five communities, located in New Haven, Connecticut, Los Angeles, California, Baltimore, Maryland, St. Louis, Missouri, and Durham, North Carolina. Despite the sample's geographic distribution, weights were eventually derived to estimate national rates of alcohol use disorders (as well as other psychiatric disorders). The study's interview, the Diagnostic Interview Schedule (DIS), was developed specifically for the ECA.

The National Comorbidity Study (NCS). The NCS was designed to provide data on the comorbidity of alcohol and other psychiatric disorders based on a full national sample. With the publication of the revision of *DSM-III* in 1987, general population data using the more recent *DSM-III-R* diagnostic criteria were needed. The interview, the University of Michigan version of the Composite International Diagnostic Interview (UM-CIDI), was developed for this survey, with various features that differentiated it from other structured diagnostic interviews (see Table 2). Another difference between the NCS and the ECA interviews was the collection of risk factor data in the NCS to offer explanations for the etiology of disorders. Test-retest studies (which measure whether two independent evaluators produce the same results from a given respondent) for alcohol disorders and drug disorders in the CIDI indicated good reliability for these diagnoses (Wittchen, 1994).

The National Longitudinal Alcohol Epidemiologic Survey (NLAES). The NLAES, the first national survey with a primary focus on *DSM*-defined alcohol use disorders, was conducted in 1992. The survey aims were to provide accurate estimates of alcohol abuse and dependence, associated physical and mental disabilities, treatment utilization, information on risk factors for substance use disorders, and the economic impact of these disorders. This required a large sample and reliable diagnostic measures. As Table 1 demonstrates, the sample was very large, exceeding 40,000 people. The diagnostic interview developed for the NLAES was the Alcohol Use Disorders and Associated Disabilities Interview Schedule, or AUDADIS (see Grant & Hasin, 1992). In the AUDADIS, alcohol dependence is not diagnosed unless symptoms cluster together chronologically. Although the NLAES was conducted prior to the publication of *DSM-IV*, the AUDADIS obtained the necessary information to make alcohol, drug, and psychiatric diagnoses according to *DSM-IV* criteria. The AUDADIS diagnoses were also subjected to test-retest reliability studies, and the results indicated good to excellent reliability for current and past alcohol disorders, and adequate to good reliability for drug disorder symptoms and diagnoses (Grant et al., 1995).

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). From 2001 to 2002, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) sponsored a survey whose sample design was similar to the NLAES, using a measurement instrument updated for *DSM-IV* (AUDADIS-IV). The NESARC included a national sample of over 43,000 respondents aged 18 and older, who were assessed for a wide range of psychiatric disorders, including alcohol disorders. Respondents were followed for three years and reassessed for psychiatric disorders from 2004 to 2005. Longitudinal studies are valuable in epidemiology because factors predicting the onset of disorder (as opposed to the prevalence of disorder) can be directly estimated without the potential for recall bias. Similar to the prior version of the AUDADIS, the updated version documented good to excellent test-retest reliability of alcohol diagnoses (Ruan et al., 2008).

National Comorbidity Study Replication (NCS-R). Part of a survey of 26 countries conducted by the World Mental Health (WMH) Survey Initiative, the NCS-R was conducted between 2001 and 2003. The NCS-R strived to study trends over time in psychiatric illness, and to update the prevalence of psychiatric disorders in accordance with the publication of the *DSM-IV*. Interview and study design features are similar enough to those of the NCS to make comparisons of the studies legitimate. An exception to this is the introduction of a new "skip feature" that eliminated all questions on alcohol and drug dependence among respondents that never met criteria for alcohol or drug abuse, respectively. A clinical

	Survey				
Disorder	**ECA**	**NCS**	**NLAES**	**NCS-R**	**NESARC**
Current*					
Any Alcohol Use Disorder	4.8	9.7	7.4	4.4*	8.5
Alcohol Abuse	1.9	2.5	3	3.1	4.7
Alcohol Dependence	2.8	7.2	4.4	1.3*	3.8
Lifetime					
Any Alcohol Use Disorder	13.5	23.5	18.2	18.6*	30.3
Alcohol Abuse	5.6	9.4	4.9	13.2	17.8
Alcohol Dependence	7.9	14.1	13.3	5.4*	12.5

*Dependence not assessed in those without abuse

Table 3. Prevalence of current and lifetime alcohol disorders in five general population surveys. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

reappraisal study was conducted using a subset of the NCS-R respondents; with the results showing adequate sensitivity for alcohol abuse but low sensitivity for alcohol dependence (63.1% and 43.1%, respectively), and excellent specificity (98.1% and 99.9%, respectively) (Kessler & Merikangas, 2004). Low sensitivity for alcohol dependence was a marked departure from the normally excellent psychometric properties of alcohol dependence measured in other major surveys, and this difference was likely due to the aforementioned skip over alcohol and drug dependence questions.

PREVALENCE OF ALCOHOL USE DISORDERS: EVIDENCE FROM PSYCHIATRIC EPIDEMIOLOGIC SURVEYS

Prevalence refers to the proportion of the population with alcohol abuse OR dependence at a given moment or period in time. Prevalence estimates are used in describing the disease burden on a population. Table 1 details the prevalence of alcohol abuse and dependence in the five major epidemiologic surveys, which estimated both current and lifetime alcohol use disorders. While estimates differ due to variations in the measurement and definition of "current disorder" and the design of the surveys (see Tables 2 and 3), these studies, "taken together," provide a comprehensive assessment of the prevalence of alcohol abuse and dependence in the U.S. population.

The prevalence of current alcohol abuse ranges from 1.9 percent in the ECA to 4.7 percent in the NESARC. Current alcohol dependence ranges from 1.3 percent in the NCS-R to 7.2 percent in the NCS. Overall, the prevalence of any current alcohol disorder ranges from approximately 4 percent to 10 percent. On a lifetime basis, estimates across surveys vary more widely. The lifetime prevalence of alcohol abuse ranges from 5.6 percent in the ECA to 17.8 percent in the NESARC, while alcohol dependence ranges from 5.4 percent in the NCS-R to 14.1 percent in the NCS. Together, these estimates indicate alcohol abuse and dependence are relatively common disorders compared to other psychiatric disorders and other chronic diseases in the population.

Because the NLAES and the NESARC used the same instrument in each survey, it is possible to examine trends over time (see Table 3). Overall, the prevalence of any current alcohol disorder increased from 7.4 percent to 8.5 percent, due mostly to an increase in the prevalence of alcohol abuse (3% to 4.7%). The prevalence of alcohol dependence decreased slightly during this period (4.4% to 3.8%). The prevalence of any lifetime alcohol disorder increased from 18.2 percent to 30.3 percent between 1991 and 1992, again due mostly to an increase in the prevalence of lifetime alcohol abuse (4.9% to 17.8%), for alcohol dependence decreased slightly (13.3% to 12.5%). Further discussion of these trends is provided by Grant and colleagues (2004).

LONGITUDINAL COURSE OF A DISORDER: ONSET, COURSE, AND RECOVERY

National surveys and longitudinal studies in both clinical and community samples have documented the course of alcohol disorders. Longitudinal studies have several advantages over cross-sectional studies in assessing the course of alcohol disorders, including minimal bias due to recall and selective mortality. However, longitudinal studies are often conducted among specialized samples, such as individuals in treatment. In general, longitudinal and cross-sectional studies concur regarding the course of alcohol use disorders.

Initiation of alcohol consumption often occurs during adolescence. Onset of alcohol abuse and dependence is most likely among individuals aged 18 to 29, although 15 percent of alcohol dependence cases begin before age 18 (Hingston et al., 2006). While alcohol abuse was once believed to be a prodromal form of alcohol dependence, evidence now suggests that over a third of those with alcohol

dependence do not meet abuse criteria (Hasin et al., 2004). In addition, longitudinal studies suggest that many individuals with alcohol abuse do not develop alcohol dependence (Hasin et al., 1990; Schuckit et al., 2005). The duration of alcohol disorders is often, but not always, chronic, with an estimated mean of nearly four years for alcohol dependence (Hasin et al., 2007).

Often, alcohol abuse and dependence are not lifelong conditions. Indeed, a high rate of recovery has been documented in general population samples, even among individuals who have never sought treatment. Studies of the general population also show that a high proportion of recovered individuals return to moderate drinking as opposed to abstinence (Tucker, 2003; Watson & Sher, 1998). Data from the NESARC indicated that approximately 75 percent of individuals diagnosed with alcohol dependence at some point in the past did not have a current (i.e., past year) diagnosis, but that only about 20 percent of these individuals were abstinent from alcohol (Dawson et al., 2004). Thus, the transition to adulthood represents a key developmental phase in which alcohol disorders often remit, in a process termed "maturing out" (Bachman et al., 2002; Dawson et al., 2006). Major predictors of recovery include key lifestyle components, such as employment, marriage, and childbirth. Whether or not these factors have a causal influence on recovery or reflect common factors underlying the positive lifestyle components and the recovery remains unknown.

Despite substantial progress in the development of treatments for alcohol disorders, only about one-fifth of those individuals with an alcohol disorder seek treatment for the condition during their lifetime (Cohen et al., 2007). Further, the delay from onset of disorder to treatment is typically eight to ten years (Wang et al., 2005). Finally, in contrast to sharp increases in treatment utilization for disorders such as depression between 1990 and 2003, a corresponding increase in the proportion of individuals seeking treatment for an alcohol disorder did not occur during this period (Kessler et al., 2005).

DEMOGRAPHIC CHARACTERISTICS AND OTHER ESTABLISHED RISK FACTORS FOR ALCOHOL USE DISORDERS

The term *risk factor* refers to a characteristic of an individual or community that influences disease risk in a population. Risk factor epidemiology is an important method used to characterize factors that influence vulnerability to alcohol abuse and dependence, and to identify subpopulations for greater intervention and prevention efforts.

Demographic Risk Factors. Alcohol use disorders are not distributed randomly in the population. On the contrary, certain demographic groups exhibit a higher prevalence of alcohol use disorders than others. Gender is a well-documented risk factor, for example. In particular, men are more likely to have alcohol use disorders than women, although evidence suggests gender differences in the prevalence of disorder have decreased over time (Keyes, Grant, & Hasin, 2007). As noted above, age is strongly related to the development of alcohol use disorders, and alcohol disorders are often exhibited in young adulthood.

Socioeconomic status is inversely related to alcohol dependence, so that individuals in lower socioeconomic groups have a higher prevalence of disorder. Alcohol abuse, conversely, is more common among individuals with higher income and educational attainment (Van Oers et al., 1999). Finally, the prevalence of alcohol use disorders varies according to a person's self-described race or ethnic group. Of the largest such groups tracked in U.S. surveys, most surveys found that Native Americans and non-Hispanic whites have the highest prevalence of alcohol disorders, while individuals of Asian descent typically have the lowest prevalence (Huang et al., 2006).

Environmental factors. A particular substance must be available in the environment for individuals to be at risk for the development of disorders involving that substance. In Western societies, competing forces influence alcohol availability. Public health, moral or religious, "grassroots," and governmental organizations attempt to reduce availability and consumption by influencing public policy and laws, while the alcoholic beverage industry attempts to increase consumption through advertising and other means. Widespread social attitudes toward alcohol use, as well as political events, also influence availability and consumption, thereby influencing the risk of alcohol use disorders.

Other external environmental factors include home and family life. Poor parental monitoring

and the modeling of heavy alcohol use contribute to the likelihood of adolescent alcohol initiation and binge drinking, although these factors may be mediators within the relationship between parental alcohol problems and adolescent alcohol use (Hawkins, Catalano, & Miller, 1992; Ellis, Zucker, & Fitzgerald, 1997; Repetti, Taylor, & Seeman, 2002). Peer influence and stressful life events are also strongly associated with adolescent alcohol abuse, while religiosity is a well-replicated protective factor (Kendler et al., 1997, Kendler et al., 2000; Walden et al., 2004; Dube et al., 2003).

Individual Risk Factors. Important risk factors for the development of alcohol disorders also exist within the individual, including positive alcohol expectancies and motivations for drinking. These beliefs and motivations can have roots in family and peer influences, but they are characteristics of the individual's internal environment. Individuals with certain personality traits, such as novelty or sensation seeking (Zuckerman & Kuhlman, 2000), may be more likely to experiment with heavy drinking, while co-occurring disorders associated with impulsivity and risk taking, such as conduct disorder and antisocial personality disorder, have been shown to predict the development of an alcohol disorder (Cloninger, Sigvardsson, & Bohman, 1988; Sher & Trull, 1994). Further, early onset of alcohol consumption is associated with a higher risk of alcohol disorder onset (Grant & Dawson, 1997; Grant et al., 2006), although evidence suggests that any early deviant behavior, including but not limited to alcohol consumption, is associated with later onset of an alcohol disorder (Kuperman et al., 2005; McGue & Iacono, 2005; King & Chassin, 2007). Thus, it is unclear whether early onset of drinking is a specific risk factor for alcohol disorders or a risk factor for a general category of externalizing behaviors.

Genetic factors are also important in the development of an alcohol disorder. Alcohol disorders are known to be familial (Cotton, 1979; Bierut et al., 1998), and twin studies of alcohol dependence show estimates of heritability (i.e., the proportion of risk attributable to genetics) of 50 percent to 60 percent (Klender et al., 2003; Heath, 1995; Rhee et al., 2003). The Collaborative Study on the Genetics of Alcoholism (COGA), a multisite family study of alcohol-dependent patients and their relatives, has contributed greatly to current knowledge of the genetic epidemiology of alcohol disorders, as have a series of case-control and family studies at Yale University and the University of Connecticut (Luo et al., 2006; Kaufman et al., 2007). In addition, linkage and association studies involving fine gene mapping have identified specific genes and alleles associated with alcohol dependence and related phenotypes through various mechanisms.

CONCLUSION

The field of epidemiology has facilitated estimates of the incidence and prevalence of alcohol use disorders and helped identify important risk factors for the onset and persistence of the disorders over time. Issues concerning major epidemiologic surveys include reliance on the self-reporting of problem behaviors and recall bias, which can affect lifetime estimates. Despite these limitations, however, epidemiologic studies present the most valid national picture of alcohol use disorders, their course, and factors associated with their occurrence. Thus, these findings play a vital role in advancing knowledge of alcohol use disorders in the general population.

See also **Alcohol: Chemistry and Pharmacology; Alcohol: History of Drinking; Alcoholism: Abstinence versus Controlled Drinking; Antisocial Personality Disorder; Diagnosis of Substance Use Disorders: Diagnostic Criteria; Diagnostic and Statistical Manual (DSM); Gender and Complications of Substance Abuse; Intimate Partner Violence and Alcohol/Substance Use; Models of Alcoholism and Drug Abuse; Prohibition of Alcohol; Research: Developing Medications to Treat Substance Abuse and Dependence; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Treatment: An Overview of Alcohol Abuse/Dependence.**

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EPIDEMIOLOGY OF DRUG ABUSE.

Epidemiology can be thought of as the cornerstone of public health research. It is a branch of biomedical science that deals with measuring the occurrence and frequency of a disease in a population, as well as identifying the causes and mechanisms. Evidence gathered in epidemiologic investigations is used to inform future prevention efforts and management of the disease. Unlike general clinical practice, epidemiology focuses on populations at risk and their subgroups rather than individuals, although individual clinical experiences can be guided by epidemiology. The epidemiology of drug abuse is concerned with describing the distribution of drug use and its associated disorders. To

do this, epidemiologists conduct surveys that seek information about all aspects of the population's drug experience and examine the intrapersonal and environmental factors that interact with each other and with genetic factors across development to identify patterns of exposure, initiation, maintenance, and desistance (i.e., cessation) of drug abuse. Furthermore, findings from epidemiologic studies can inform clinical practice, prevention programs, and other health and social services as avenues to improve public health.

There is, of course, good reason to wonder whether epidemiologic surveys of drug use and drug dependence have sufficient validity to be trusted. On the one hand, especially among young people, there may be a tendency to exaggerate drug taking, and to falsify survey responses in the direction of more drug taking than has really occurred. On the other hand, some people may be hesitant to disclose their histories of drug taking or drug problems; they might not agree to participate in the survey, or they might falsify their answers in the direction of less drug taking or fewer problems than have actually occurred.

Fortunately a body of methodologic research provides general assurance about the accuracy of estimates in drug abuse epidemiologic surveys. Accuracy of the survey results seems to be enhanced considerably when special care is taken to guarantee confidentiality of responses, to protect the privacy of the survey respondents, and to develop trust and rapport before asking survey questions about sensitive behavior, alcohol and drug problems, or illegal activities. In particular, except in poorly conducted surveys of very young respondents, there seems to be very little exaggeration of drug involvement, and older adolescents and adults rarely report drug use unless it actually has happened. Moreover, the accuracy of the estimates does not seem to be distorted greatly when the surveys concentrate on household residents and do not extend their samples to include homeless or imprisoned segments of the population. Although homeless people and prisoners often have significant and special needs for alcohol- and other drug-dependent treatment services that society cannot ignore without peril, the number of homeless and incarcerated persons is small relative to the considerably larger number of persons living in households.

It also is important to note the relatively large size of the survey estimates obtained in these epidemiologic surveys. For example, in 2007, as part of the annual Monitoring the Future (MTF) study, more than fifteen thousand high school seniors were asked to fill out confidential questionnaires about their use of such drugs as marijuana, cocaine, and nonmedical use of prescription drugs; about 47 percent reported having taken any illicit drug, 72 percent reported consuming alcoholic beverages, and 55 percent reported having consumed alcohol to the point of getting drunk. The same study also surveyed roughly thirty-four thousand tenth and eighth graders, and lifetime illicit drug use was reported by more than one-third and one-fifth, respectively, of these students. In 2006, nearly sixty-eight thousand American household residents aged twelve years and older participated in a U.S. government-sponsored National Survey on Drug Use and Health (NSDUH) and were asked to answer an interviewer's questions about the use of these drugs; illegal drug taking was reported by an estimated 28 percent of those twelve to seventeen years, 59 percent of those eighteen to twenty-five, and 46 percent of those twenty-six and older.

Furthermore, between 2001 and 2002 more than 43,000 Americans over the age of eighteen completed confidential interviews as part of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). With the NESARC it is possible to estimate the proportion of drug users who have developed drug disorder syndromes, as defined in relation to *DSM-IV*, a set of diagnostic criteria for drug abuse or dependence that were developed by the American Psychiatric Association in 1994. Before the diagnoses of drug abuse or dependence are made, the survey must produce evidence that drug users experienced signs or symptoms of disorder such as unsuccessful efforts to cut down, recurrent social or interpersonal problems resulting from drug use, going through withdrawal, or taking drugs to avoid withdrawal symptoms. As such, 10 percent of the adults surveyed showed evidence of at some point having a drug use disorder (abuse or dependence).

While estimates across these surveys often tend to vary slightly, it must be noted that these surveys have methodological differences, including

population structure under study, mode and location of administration, questionnaire wording, and response rates, among others (see Anthony & Helzer, Epidemiology of Alcohol Abuse and Dependence [2007] for a detailed description of methodologic features of recent national surveys of substance use and disorders). Despite the wide range of possible discrepancies, the trends in drug use reported by these surveys tend to be consistent over time, and unique characteristics of the individual surveys can be combined for an accurate picture of illicit drug abuse. Further, even if under-reporting were an issue, these survey-based estimates are already high enough to provoke social concern.

DRUG-SPECIFIC ESTIMATES FOR THE U.S. POPULATION

It may be useful if, bearing in mind the potential limitations in the survey methods, one considers each broad drug class one by one, in order to convey the relative frequency of use of tobacco, alcohol, and other drugs in the United States, and to identify population subgroups within which drug use or drug dependence are most common. The estimates presented here are from the 2007 MTF, 2006 NSDUH, and 2001–2002 NESARC surveys. In view of recent attention to the caffeine-dependence syndrome and other health effects of drinking coffee, tea, "energy" drinks or consuming other caffeinated products, estimates concerning the use of caffeine and caffeine dependence might seem warranted. However there is not yet a stable base of epidemiologic data on caffeine use and caffeine dependence. These are among the topics that ought to be examined in future epidemiologic studies.

Tobacco Smoking. Monitoring the Future (MTF) estimates show that about 46 percent of high school seniors have smoked tobacco cigarettes at least once in their lifetime. An estimated 22 percent of high school seniors smoked tobacco cigarettes at least once during the month prior to the survey, and about 12 percent were daily tobacco smokers.

According to the NSDUH, which included household residents age twelve years and older, an estimated 66 percent smoked tobacco cigarettes at least once, for a total of about 162,991,000 smokers. An estimated 29.1 percent had smoked in the year prior to the survey, for a total of 71,676,000 recently active smokers; most of these had smoked in the month prior to the survey (25%; 61,565,000).

There are some important age- and sex-related variations in these NSDUH estimates. For example, 40 percent of young adults aged twenty-one to twenty-five reported current cigarette use, while 23 percent of adults age thirty-five or older were current smokers. While the rate of current cigarette smoking was similar for male and female youth aged twelve to seventeen, current use of any tobacco product among respondents aged twelve and older was reported by more males than females (36% vs. 23%, respectively). Among young adults eighteen to twenty-five, within the limits of survey error, there were differences between the sexes with an estimated 42 percent of males and 35 percent of females reporting smoking, and among those past age twenty-five, males were more likely than females to have been recent tobacco smokers (27.8% versus 21.8%).

Smokeless Tobacco Use. An estimated 15 percent of high school seniors had tried smokeless tobacco at least once, and about 6.6 percent had used it during the month prior to the survey (MTF estimates). NSDUH estimates indicate somewhat lower values for smokeless tobacco, except among males aged eighteen to twenty-five. For example, among twelve- to seventeen-year-olds, an estimated 7.1 percent had tried smokeless tobacco, and 2.4 percent had used it in the month prior to the survey. By comparison, about 20 percent of eighteen- to twenty-five-year-olds and individuals age twenty-six and older had tried smokeless tobacco. Males were much more likely to have tried smokeless tobacco (32.3% vs. 5.7% for females) and be recent users; 6.6 percent had used it during the month prior to the survey, while an additional 8.8 percent had used it at some time before the past month.

Alcohol Use. An estimated 72.2 percent of high school seniors have consumed alcohol at least once. About 66.4 percent had consumed alcoholic beverages in the year prior to the survey, and about 44.4 percent had done so during the month prior to the survey. Just over 3 percent had become daily drinkers (MTF estimates). An estimated 55.1 percent of high school seniors had been drunk at least

once—about 46.1 percent during the year prior to the survey and almost 29 percent during the month prior to the survey. Nearly 30 percent had consumed five or more drinks in a row in the two weeks prior to the survey (an indicator of binge drinking), and just over 1 percent reported getting drunk daily (MTF estimates).

Among household residents aged twelve and older, an estimated 82.7 percent had consumed alcoholic beverages; this represents 203,368,000 individuals. During the month prior to the survey, an estimated 51 percent had consumed alcohol. As might be expected, the prevalence values for eighteen- to twenty-five-year-olds were somewhat higher than they were for the high school seniors, especially in relation to recent drinking: Almost 62 percent of the eighteen- to twenty-five-year-olds had consumed alcoholic beverages during the month prior to the survey. The values for twelve- to seventeen-year-olds were lower: About 40.4 percent in this age group had tried alcoholic beverages at least once, and about 16.6 percent had consumed alcohol during the month prior to the survey (NSDUH estimates).

An estimated 22.4 percent of respondents of all age groups from twelve years upward reported drinking at least once per week during the year prior to the survey. Corresponding estimates for respondents aged 12 to 17, 18 to 25, 26 to 34, and 35+ were 4.6, 24.5, 23.8, and 24.6 percent, respectively (NSDUH estimates).

Alcohol dependence was found to have affected 15 percent of those who had consumed alcoholic beverages: Of every six or seven persons who had tried alcohol, about one had become dependent on it. In relation to the total survey population that included drinkers as well as abstainers, an estimated 12.5 percent were found to qualify for the diagnosis of alcohol dependence, according to the *DSM-IV* criteria (NESARC estimates).

ILLICIT DRUG USE

When controlled substances such as marijuana, cocaine, and heroin, as well as inhalant drugs, were considered, it was found that an estimated 49 percent of respondents had used these drugs on at least one occasion, 37 percent during the year prior to the survey. About 23 percent had taken one or more of these drugs during the month prior to the survey (MTF estimates).

The NSDUH reported that an estimated 45.4 percent of the population aged twelve and older had engaged in illicit drug use at least once; this amounts to approximately 111,774,000 drug takers. The number of recently active drug takers was lower; past month users represented 8.3 percent of the population (NSDUH estimates).

According to the NESARC estimates, of every eight or nine persons who had tried marijuana, cocaine, hallucinogens, opioids, or other controlled substances and inhalant drugs, one had developed drug dependence (11.4%). In the total population of individuals (including both drug users and never users), 2.6 percent had fulfilled the criteria for drug dependence (NESARC estimates).

Cannabis Use. An estimated 42 percent of high school seniors had tried marijuana or hashish (*Cannabis*) on at least one occasion, and about 32 percent had smoked cannabis during the year prior to the survey. An estimated 19 percent had smoked cannabis during the month prior to the survey, and an estimated 5 percent reported daily cannabis use (MTF estimates).

Within the age range of twelve to seventeen, there are many individuals who have not yet started to use illicit drugs such as cannabis, as well as many others who never will start to use these drugs. As a result, one might expect a lower prevalence value in this age group as compared to the values for other age ranges. In fact, this is precisely what the national survey estimates indicate. Overall, an estimated 39.8 percent of respondents reported having tried cannabis, but among twelve- to seventeen-year-olds the estimate was only 17.3 percent, and among those aged twenty-six years and older it was 40.6 percent. Prevalence of cannabis use was most common among eighteen- to twenty-five-year-olds (52.4%). This also was true for recent cannabis use during the month prior to the survey: There was a prevalence of 6.0 percent for the population overall, 6.7 percent for twelve- to seventeen-year-olds, 16.3 percent for eighteen- to twenty-five-year-olds, and 4.2 percent for older adults (NSDUH estimates).

Among cannabis users, about 6.3 percent were found to have developed cannabis dependence. Also noteworthy, is that more than one-third of

cannabis users also had a history of lifetime alcohol dependence. Among all respondents aged 18 and older (including both users and never users), 1.3 percent had become dependent on cannabis (NESARC estimates).

Inhalant Use. Inhalants had been used by an estimated 11 percent of high school seniors—about 4 percent within the year prior to the survey and just over 1 percent during the month prior to the survey. Unlike other illicit drugs assessed in this survey, inhalant use is more prevalent in the younger rather than older students; one in every six or seven eighth graders reported having used inhalants (MTF estimates).

The National Household Survey on Drug Abuse indicated that about 9.3 percent of its survey population had tried inhalants at least once; about 1 percent had done so during the year prior to the survey, and about 0.3 percent had used these drugs during the month prior to the survey. It was found, when considering age and sex, that the subgroup most likely to have used inhalant drugs during the month prior to the survey was that of females aged twelve to seventeen; in this group, 1.5 percent reported recently active inhalant use (NSDUH estimates).

An estimated 19 percent of the inhalant users have been found to qualify for the diagnosis of an inhalant disorder (abuse or dependence, although dependence was virtually nonexistent in the NESARC sample). Translated into an overall prevalence estimate for both users and nonusers, this amounts to about 0.3 percent of inhalant disorder in the total survey population (NESARC estimates).

Use of Psychedelic Drugs. Psychedelic drugs (hallucinogens) had been used by an estimated 8.4 percent of high school seniors. Around 5.4 percent of high school seniors had used them in the year prior to the survey, and about 1.7 percent had used them during the month prior to the survey. Some of the more commonly used types of hallucinogens are MDMA (methylenedioxymethamphetamine, or "Ecstasy"), lysergic acid diethylamide (LSD), and phencyclidine (PCP). Nearly 7 percent of twelfth graders reported use of MDMA, 3.4 percent used LSD, and PCP users were in the minority within this group of drug users—only 2.1 percent of the high school seniors had ever tried PCP (MTF estimates).

Among persons aged twelve years and older, around 14.3 percent of individuals had tried psychedelic drugs such as LSD, but for the most part these drug experiences were not recent: Only 0.4 percent reported taking psychedelic drugs during the month prior to the survey. Peak prevalence values for recent use of the psychedelic drugs were observed in the years of adolescence and early adulthood; only for eighteen- to twenty-five-year-olds did these values exceed a threshold of 1 percent (1.7%); otherwise, they were at the 0.7 percent level or lower (NSDUH estimates).

About 0.2 percent of adults aged eighteen and older surveyed in the NESARC had become dependent on psychedelic drugs, defined in relation to the American Psychiatric Association criteria.

Cocaine Use. Among high school seniors, an estimated 7.8 percent had tried cocaine; within this group of cocaine users, almost one-half had tried crack-cocaine (3.2%). About 5.2 percent of high school seniors had used cocaine (including crack) during the year prior to the survey, and 2.0 percent had used it in the month prior to the survey (MTF estimates).

An estimated 14.3 percent of the NSDUH population reported having tried cocaine or crack smoking (or both) at least once. The corresponding value for twelve- to seventeen-year-olds was only 2.2 percent, and there was age-related variation: 15.7 percent of the eighteen- to twenty-five-year-olds had taken cocaine (including crack) while the prevalence estimate for older adults was 15.8 percent. Translated into absolute numbers, an estimated thirty-five million Americans aged twelve and older had used cocaine (or crack). Recent use was substantially less common: Only 1.0 percent of the survey population reported having used these drugs during the month prior to the survey; this represented about 2.4 million recently active cocaine users in the United States.

The relatively low prevalence values for crack smoking among high school seniors was reflected in the NSDUH, which found that only 3.5 percent of its survey population had tried crack smoking; this amounted to more than 8.5 million

individuals. The age groups with most crack-smoking experience were the twenty-six-year-olds and older, with a prevalence value of 3.9 percent. Prevalence of crack smoking during the month prior to the 2006 survey was 0.3 percent or lower for all age and sex groups under study (NSDUH estimates).

For every six individuals who had tried cocaine at least once, one had developed cocaine dependence. That is, among cocaine users, an estimated 16 percent had become sufficiently dependent upon cocaine to qualify for the American Psychiatric Association diagnosis. Nearly half of all cocaine users also had a diagnosis of alcohol dependence, and more than a quarter had some type of drug dependence diagnosis. In relation to all persons in the survey population, whether they had tried cocaine or not, an estimated 1 percent qualified for the diagnosis of cocaine dependence (NESARC estimates).

Use of Non-Cocaine Stimulants. The nonmedical use of stimulants other than cocaine (such as amphetamines) was actually more prevalent than cocaine use among high school seniors. An estimated 11.4 percent of high school seniors had taken these stimulant drugs without any doctor's orders; 7.5 percent had done so in the year prior to the survey, and 3.7 percent had done so during the month prior to the survey. Ritalin, a stimulant used therapeutically for the management of Attention Deficit Hyperactivity Disorder (ADHD), had been used nonmedically by nearly 4 percent of seniors in the year prior to the survey. Among high school seniors, 3.4 percent had ever tried crystal methamphetamine ("ice"), 1.6 percent had done so in the year prior to the survey, and 0.6 percent had used during the prior month (MTF estimates).

Overall, the NSDUH population estimate for nonmedical use of these stimulant drugs was 8.2 percent, and the age group with the highest prevalence value was that made up of eighteen- to twenty-five-year-olds, at 10.7 percent. Within the survey population, recent use of the stimulant drugs was found to be 3.8 percent for the eighteen- to twenty-five-year-olds (NSDUH estimates).

Among adults surveyed in the NESARC, 4.7 percent reported any nonmedical use of amphetamines, and the corresponding rate of disorder (abuse and/or dependence) was 2 percent (NESARC estimates).

Use of Anxiolytic, Sedative, and Hypnotic Drugs. About 9.3 to 9.5 percent of high school seniors had used tranquilizers (anxiolytic) or sedative-hypnotic (e.g., barbiturate) drugs without a doctor's orders. About 6.2 percent had done so during the year prior to the survey, and nearly 27 percent had done so during the month prior to the survey (MTF estimates, sedatives and tranquilizers reported separately).

About 8.7 percent of the NSDUH survey population reported nonmedical use of tranquilizers or anxiolytic drugs, while 3.6 percent reported nonmedical use of sedative-hypnotic drugs. For tranquilizers, this amounted to more than twenty-one million people using these drugs without a doctor's orders. For sedative-hypnotics, the total was 8.8 million nonmedical users. The estimated number of recently active users was less substantial; they represented 0.7 percent of the survey population for tranquilizers (1,766,000 nonmedical users) and 0.2 percent for the sedative-hypnotics (385,000 nonmedical users).

About 4 percent of adults surveyed in the NESARC had used sedatives nonmedically and around 0.3 percent had been diagnosed with dependence on sedatives. Similarly, 3.4 percent had used tranquilizers and 0.2 percent qualified for a diagnosis of dependence (NESARC estimates).

Use of Opioid Drugs. Any use of heroin was reported by 1.5 percent of high school seniors, with less than 1 percent using in the twelve months prior to the survey. Other opioid drugs often prescribed for the management of pain, such as oxycodone or hydrocodone, are being diverted to nonmedical use and an estimated 13 percent of twelfth graders report trying one of these drugs without a doctor's orders. In other words, more than one of every eight high school seniors have used these prescription opioids nonmedically (MTF estimates).

Similar to the twelfth grade estimates from MTF, 1.5 percent of the national household population aged twelve and older had used heroin at some time, and 0.2 percent or fewer had used within the year prior to the survey. Lifetime use

peaks in early adulthood, where 2.4 percent of adults aged twenty-six to thirty-four had tried heroin. Nearly 14 percent of the sample surveyed have tried painkillers for nonmedical purposes, and about 5 percent had been using in the year prior to the survey (NSDUH estimates).

Nearly 5 percent of adults aged eighteen and older surveyed in the NESARC had used opioids nonmedically and 1.4 percent received a diagnosis of use disorder (abuse and/or dependence) (NESARC estimates).

TRENDS AND CURRENT ISSUES

One of the major benefits of these annual epidemiologic surveys is that they can paint a picture of historical, current, and emerging trends in relation to drugs of abuse. Trends tend to be complex and cycle based on the experience of a particular age cohort, as new drugs enter the scene and older drugs re-emerge among young people who have yet to experience the adverse consequences in their generation. For example, by the early 1990s, the second American epidemic of cocaine use had peaked, sustained for some time by crack smoking, and waned by the early 1990s when it became clear that crack smoking had not diffused broadly through the U.S. population. As illustrated by crack smoking, non-injecting heroin use, and crystal methamphetamine (ice), oftentimes the introduction of "new" drugs is merely a new formulation or mode of administration for drugs that have been around for generations.

Throughout this decade, abuse of prescription medications has emerged as one of the most prevalent categories of illicit drug use. Increased availability to consumers and perhaps a lower awareness of the risks of these drugs because they can be prescribed by doctors are just two of the factors that have brought abuse of these medications into the mainstream. More than one in five high school seniors had tried a prescription psychotherapeutic medication at least once without a doctor's orders, 15.4 percent in the year prior to the survey and nearly 8 percent in the month prior (MTF estimates). Similar estimates were reported by household residents aged twelve and older, suggesting that nearly fifty million people have used these medicines for nonmedical reasons (NSDUH estimates).

Despite this entry's unilateral focus on drug abuse there exists a high degree of comorbidity associated with drug use. Comorbidity refers to the occurrence of two or more substance or psychiatric disorders within a certain period of time, and there is a history of epidemiologic surveys such as the Epidemiologic Catchment Area (ECS) study, National Comorbidity Survey (NCS), and the NESARC that have shown mood, anxiety, and personality disorders to be related to drug use and disorders. These findings also have important implications for prevention and control of drug abuse, as it makes the course of these disorders more complex and often more chronic.

EPIDEMIOLOGY OF DRUG USE AND DRUG DEPENDENCE OUTSIDE THE UNITED STATES

Each year, the United States allocates more resources to epidemiologic surveys of drug use than does any other country in the world. For this reason, it has been possible to assemble a wealth of epidemiologic survey data on the prevalence of drug use and drug dependence within the United States. Other countries also have conducted surveys of this type and have produced valuable evidence about their experience with tobacco, alcohol, and other drugs. States, countries, and continents vary dramatically as to which drugs of abuse are more problematic than others, in terms of use as well as production and trafficking.

Of great concern globally is the transmission of HIV/AIDS through injection drug use; up to 10 percent of all HIV infections around the world could be attributable to injection drug use, and in some areas such as Eastern Europe or Central and Southeast Asia injection drug use might account for up to 80 percent of the cases of HIV. (See the bibliography for some references that can be consulted to gain more information about the results of these surveys.)

OTHER ASPECTS OF EPIDEMIOLOGY AS APPLIED TO DRUG USE AND DRUG DEPENDENCE

A broad range of research questions must be answered in order to gain a complete understanding of the epidemiology of drug use and drug dependence. The focus in this entry has been on quantity, or measuring the occurrence or

frequency of drug abuse. Although many epidemiologists now devote their research careers to surveys that are needed to answer this kind of basic question, more stress ought to be placed on the other central aspects of epidemiology or aspects of public health that epidemiology can inform. These include the following:

- Location, identifying where and within which population subgroups cases are more likely to arise. Location can incorporate geography, season, culture or society, or year in history in which drug involvement is examined. Interaction of geographical context, environmental, social, and economic factors and how they contribute to the etiology of drug abuse is one avenue that can inform this aspect of epidemiology.
- Investigation of causes, determining what accounts for some people or populations, but not others, becoming affected. For example, family history has consistently been identified as a compelling risk factor for drug use and abuse, but does not guarantee that future generations will be affected. Advances in research of the interplay between genes and environment, such as studying the effects of the environment on gene expression (epigenetics), heritability, and gene-environment correlations and interactions, and how all these influences change throughout development, are helping scientists understand the causes of complex disorders like drug abuse and dependence.
- Studies of linked sequences of causal conditions (i.e., mechanisms) as they relate to drug dependence explore the natural history and clinical course of drug use as it proceeds from exposure to initiation to disorder to remission.
- Finally, *prevention and treatment* of drug abuse can improve the public's health and reduce the burden caused by drug disorders.

At its best, epidemiology contributes critically important evidence to each of these rubrics, and it works to ensure that new findings are translated rapidly into effective strategies for prevention. This is the future agenda for epidemiologic research on drug use and drug dependence.

See also **Amphetamine Epidemics, International; Diagnosis of Substance Use Disorders: Diagnostic Criteria; Diagnostic and Statistical Manual (DSM); Drug Abuse Warning Network (DAWN); Epidemics of Drug Abuse in the United States; Social Costs of Alcohol and Drug Abuse.**

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ETHCHLORVYNOL. This is a complex alcohol that causes depression of the central nervous system (CNS). It is a sedative-hypnotic drug typically used on a short-term basis to treat insomnia and is prescribed and sold under the name Placidyl. Because of its depressant effects on the brain, it can impair the mental and/or physical abilities necessary to operate machinery, such as an automobile.

Continued use of ethchlorvynol can result in tolerance and physical dependence leading to abuse. Since the risk of abuse is not very great, it is included in Schedule IV of the Controlled Substances Act. Withdrawal signs, not unlike those seen after alcohol (ethanol) or barbiturates, occur upon termination of its use in addicts. Ethchlorvynol should never be combined with other CNS depressants, such as ethanol or barbiturates, because their depressant effects are additive. Because of their greater safety, the widespread use of benzodiazepines as sedative/hypnotics has largely supplanted the use of ethchlorvynol.

See also **Withdrawal.**

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ETHINAMATE. This is a short-acting sedative-hypnotic drug typically used to treat insomnia. It is prescribed and sold as Valmid. Structurally, it does not resemble the barbiturates, but it shares many effects with this class of drugs; the depressant effects of ethinamate are, however, generally milder than those of most barbiturates. Continued and inappropriate use of ethinamate can lead to tolerance and physical dependence, with withdrawal symptoms very similar to those of the barbiturates. Because of their greater safety, the widespread use of benzodiazepines as sedative/hypnotics has largely supplanted the use of ethinamate.

See also **Withdrawal.**

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ETHNICITY AND DRUGS. *See* **African Americans, Ethnic and Cultural Factors Relevant to Treatment for; Chinese Americans, Alcohol and Drug Use Among; Hispanic Americans, Alcohol and Drug Use Among; Jews and Alcohol; Racial Profiling.**

ETHNOPHARMACOLOGY. This branch of pharmacology studies the use and lore of drugs that have been discovered and developed by sociocultural (or ethnic) groups. It involves the direct observation and report of interactions between the societies and the drugs they have found in their natural environments and the customs that have evolved around such drugs, whether ceremonial, therapeutic, or other. These drugs, usually found in plants (hence similar study by ethnobotanists as well as ethnologists), are described—

as are their effects within the customs, beliefs, and histories of a traditional culture or a specific society.

Examples include descriptions of the use of coca leaves (*Erythroxylon coca*) by indigenous populations of Colombia and Peru, for increased strength and endurance in high altitudes; the ceremonial use of peyote (*Lophophora sp.*) by Native Americans of the Southwest and Mexico; and the use of kava (*Piper methysticum*) in ceremonial drinks by the indigenous populations of many South Pacific islands.

See also **Dover's Powder; Plants, Drugs From.**

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EUROPEAN UNION. The European Union (EU) is a supranational organization created by a series of treaties. The twenty-seven member states pool their sovereignty to make joint decisions through shared institutions, such as the European Parliament, which is elected by EU citizens, and the Council of the European Union, which represents national governments. Representing the interests of the EU as a whole, the European Commission makes proposals for legislation and enforces the laws that have been adopted by the Council and Parliament. The European Court of Justice ensures that EU law is complied with, and that the various treaties are correctly interpreted and applied. The European Community began as the European Coal and Steel Community in 1952. This "community" was established to achieve the political goal of peace and the economic goal of a common market. During these early years, the European Community had only limited concern for occupational health, and it did not have the legal authority to engage in public health issues. Successive treaties have further unified the member states and expanded the competences to include a wide range of policy areas, including health policy.

The European Community started sponsoring public health education campaigns in the 1970s. However, the Community's first major public health initiative, the Europe Against Cancer Program (EACP), was not established by the Council until July 1986. The main components of this program were cancer prevention, information and public awareness, and training (Hervey, 2002). Within this mandate, the EACP developed legislative proposals for tobacco control, funded the Bureau for Action on Smoking Prevention (BASP), and encouraged the coordination of national cancer groups. In 1993, the Treaty of Maastricht expanded the authority of the community to establish the EU and included an article providing an explicit legal basis for health initiatives. However, Article 129 of the treaty still limited the EU to contributing "towards a high level of human health protection by encouraging cooperation between Member States, and, if necessary, lending support to their action."

In 1999, the Treaty of Amsterdam amended and renumbered the public health section of the Treaty of Maastricht, creating the current Article 152, which defines the role of the EU as complementing national policies, setting out procedures by which the EU institutions may act in the health field, and delineating the types of measures that may be enacted. Member states retain responsibility for the organization and delivery of health services and medical care. The EU Treaty is known as "primary legislation" because it gives the EU the authority to act. Secondary legislation consists mainly of regulations, directives, and recommendations adopted by the EU institutions. Although EU legislation sets minimum excise duties and product definitions for alcohol and tobacco, member states define their own tax structures. Thus, taxes and prices for alcohol and tobacco vary widely among member states.

To reduce the burden of disease and promote the health of the general population, the European Commission has developed a coordinated approach

1. A high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities.
   Community action, which shall complement national policies, shall be directed towards improving public health, preventing human illness and diseases, and obviating sources of danger to human health. Such action shall cover the fight against the major health scourges, by promoting research into their causes, their transmission and their prevention, as well as health information and education.
   The Community shall complement the Member States' action in reducing drugs-related health damage, including information and prevention.
2. The Community shall encourage cooperation between the Member States in the areas referred to in this Article and, if necessary, lend support to their action.
   Member States shall, in liaison with the Commission, coordinate among themselves their policies and programmes in the areas referred to in paragraph 1. The Commission may, in close contact with the Member States, take any useful initiative to promote such coordination.
3. The Community and the Member States shall foster cooperation with third countries and the competent international organisations in the sphere of public health.
4. The Council, acting in accordance with the procedure referred to in Article 251 and after consulting the Economic and Social Committee and the Committee of the Regions, shall contribute to the achievement of the objectives referred to in this article through adopting:
   (a) measures setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives; these measures shall not prevent any Member State from maintaining or introducing more stringent protective measures;
   (b) by way of derogation from Article 37, measures in the veterinary and phytosanitary fields which have as their direct objective the protection of public health;
   (c) incentive measures designed to protect and improve human health, excluding any harmonisation of the laws and regulations of the Member States.
   The Council, acting by a qualified majority on a proposal from the Commission, may also adopt recommendations for the purposes set out in this article.
5. Community action in the field of public health shall fully respect the responsibilities of the Member States for the organisation and delivery of health services and medical care. In particular, measures referred to in paragraph 4(a) shall not affect national provisions on the donation or medical use of organs and blood.

Table 1. Treaty of the European Union, Public Health Article 152. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

to addressing major health determinants, including the harmful usage of illicit drugs, alcohol, and tobacco. The Health and Consumer Protection Directorate-General (DG) is primarily responsible for health policy within the Commission. EU health policy was first set out in the European Community health strategy put forward in May 2000. A new health strategy, outlined in the white paper "Together for Health: A Strategic Approach for the EU 2008–2013," was adopted on October 23, 2007. There are two main goals of this strategy. The first is to encourage and support the development of actions and networks for compiling, reporting, and exchanging information to evaluate and define policies, strategies, and programs, with the purpose of establishing effective health interventions. The second is to promote and stimulate member states' efforts to reduce negative health impacts through the regulation of harmful substances, information and education campaigns, and treatment programs.

TOBACCO

Following the EACP, EU tobacco policies have been criticized for the inconsistent objectives of reducing the negative health impacts of tobacco while simultaneously subsidizing tobacco farmers and protecting tobacco industry jobs. The EU is one of the largest cigarette manufacturing regions in the world, and there is an extensive export market. Subsidies for tobacco farmers were approximately one billion euros (US $1.5 billion) in 2005. These subsidies are being phased out, however, with a target date of 2010, and the Common Agricultural Policy (CAP) that manages the tobacco subsidy is encouraging sustainable economic development by rewarding the transition to healthful products and developing alternative sources of income and economic activity (European Commission, 2008). This shift toward public health policies taking precedent over agricultural interests stems from the fact that tobacco-related diseases are the single largest cause of death in Europe (ASPECT Consortium, 2004).

After the first wave of tobacco-control legislation, including taxation, directives on regulation, and an attempted ban on advertising, the tobacco industry implemented their own comprehensive lobbying strategy (Gilmore & Mckee, 2004). The industry's well-funded and multidimensional approach included the creation of the Confederation of European Community Cigarette Manufacturers, the funding of smokers' rights groups, and the support of research facilities. Tobacco industry documents later revealed close associations with both national government officials and EU staff. In particular, tobacco lobbyists encouraged and supported the German government's successful legal challenge overturning the EU's first Tobacco Advertising Directive in 2001. The German government complained that the official legal basis for the directive, the regulation of the single European market, did not support a total tobacco advertising

Public Health Agency	Created in January 2005 to manage all the phases of specific projects funded under the Program; to execute the budget for all operations necessary for the management of the Program; and to provide logistical, scientific and technical support for meetings and conferences. http://ec.europa.eu/phea/what_is_phea/what_is_phea_en.html
European Monitoring Centre for Drugs and Drug Addiction	Inaugurated in 1995, the EMCDDA is the hub of drug-related information in the European Union. It exists to provide the EU and its Member States with a factual overview of European drug problems and a common information framework to support the drugs debate. http://www.emcdda.europa.eu/
European Foundation for the Improvement of Living and Working Conditions EUROFOUND	Established in 1975, to collect information advice and expertise—on living and working conditions, industrial relations and managing change in Europe—for key actors in the field of EC social policy on the basis of comparative information research and analysis. http://www.eurofound.europa.eu/

Table 2. Selected health-related European Union agencies. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

ban. The European Court of Justice agreed, and found that the EU Treaty did not provide legal authority to justify the ban on public health grounds. The Commission quickly drafted a new directive, which was submitted to the Parliament and Council for approval. Negotiations were again strained, with Germany firmly supporting the tobacco industry's interests. Agreement on the new directive was not reached until November 2002, when the Parliament passed a watered-down draft. Thus, the Tobacco Advertising Directive (*Directive 2003/33/EC on the Approximation of the Laws, Regulations and Administrative Provisions of the Member States Relating to the Advertising and Sponsorship of Tobacco Products*) was ultimately adopted without the support of Germany and the United Kingdom. The Court rejected Germany's second legal challenge, ruling that the measures in the directive were appropriate for achieving the stated objectives.

The primary laws now regulating the tobacco market in the EU are the 2003 Tobacco Advertising Directive and the 2001 Tobacco Products Directive (*Directive 2001/37/EC on the Approximation of the Laws, Regulations and Administrative Provisions of the Member States Concerning the Manufacture, Presentation and Sale of Tobacco Products*). The Products Directive requires high-visibility, hard-hitting health warnings on all tobacco products sold in the EU, and misleading descriptors such as "light," "ultra light," and "mild," which give the impression that certain types of cigarette are less dangerous, are banned. The directive also regulates maximum levels of tar, nicotine, and carbon monoxide in cigarettes. The Advertising Directive bans all tobacco advertising on the radio, the Internet, and in the print media in EU countries, and it prohibits tobacco sponsorship of cross-border events. The directive is limited, however, in that it does not cover advertising in cinemas, on billboards, or at strictly local sporting events. In April 2006 the European Commission sent formal notice of noncompliance to the Czech Republic, Italy, Hungary, and Spain for failure to enforce the Tobacco Advertising Directive. These states must bring their legislation into conformity with the directive or face infringement procedures (European Commission, 2006a). (For a detailed comparison of tobacco control legislation in thirty European countries, see the report written by Luk Joossens and Martin Raw in 2007.) As of 2007, all EU members have signed the Framework Convention on Tobacco Control (FCTC), and all but two have ratified the convention.

The EU has also sponsored significant antismoking media and education campaigns. From 2002 to 2004 the €18 million "Feel Free to Say No" antismoking campaign included television advertising geared toward adolescents. An evaluation of the campaign disclosed the need for more narrowly targeted strategies and greater focus on the independence of youth and the risks of addiction (Evalua, 2003). In 2005 the Commission launched a new campaign, "HELP—For a Life without Tobacco" with a budget of 72 million euros (US $113 million). This multimedia Europe-wide campaign includes Web-based advertising, more nationally tailored messaging, and information about the dangers of exposure to environmental smoke.

Policy trends in the EU have focused on encouraging member states to enact legislation

expanding smoking bans in public places and requiring health labels to include color pictures. In an Annex to *Commission Decision 2003/641/EC on the Use of Color Photographs or Other Illustrations as Health Warnings on Tobacco Packages*, in accordance with Article 5 of the Products Directive, the Commission adopted a library of forty-two selected source documents and technical specifications for printing combined pictorial and written warnings. Member states have also been encouraged to use combined warnings that include quitline phone numbers, Internet addresses, or other visual elements informing smokers about the support available to whose who want to stop smoking. However, a 2007 Commission report found that only Belgium, Romania, and the United Kingdom had plans to implement the combined pictorial warnings by autumn 2008 (European Commission, 2007e).

In 2007 the Commission published a green paper examining the health and economic burdens associated with passive smoking, public support for smoking bans, and the measures taken so far at national and EU level (European Commission, 2007b). The Commission had invited stakeholders to express their views on the scope of measures available to address the dangers of passive smoking and the most appropriate form of EU intervention. The responses verified that only a full smoking ban in all enclosed workplaces and public places could adequately protect the health of citizens and workers. However, mechanisms to achieve this goal must be addressed at both the member state and the EU level. The paper concluded that the EU should provide support in cases where national governments encounter political difficulties introducing comprehensive smoke-free legislation in the hospitality and leisure sector.

Cigarette smuggling into and across Europe has continued to be a problem since the creation of the Single European Market. On March 18, 2008, the European Anti-Fraud Office (OLAF) announced the arrest of twenty-six people in Poland and Germany, including the presumed main organizers of an international criminal gang responsible for smuggling millions of cigarettes into the EU from former Soviet Union countries and China. In addition to the arrests, the authorities in Poland seized nearly seven million cigarettes, a truck that was in the process of being loaded with contraband cigarettes, nearly three million euros in cash, and nine kilos of gold and jewelry (European Anti-Fraud Office, 2008).

ALCOHOL

The EU has the highest level of alcohol consumption in the world, with 11 liters of pure alcohol drunk per adult per year (Anderson & Baumberg, 2006). Alcohol has been produced and consumed in Europe for thousands of years, and it is deeply intertwined with many local cultural traditions. Prior to the major EU expansion in 1995, the European Commission defined alcohol as either an industrial or an agricultural product. Only distilled spirits were regulated as an alcoholic beverage, but the powerful Amsterdam Group, representing large international alcohol corporations, has effectively protected the industry's interests for many years (Kurzer, 1998).

The European Court of Justice has also played an active role in the harmonization of alcohol control regulations among member states. In two 2004 cases regarding the French ban on alcohol advertising on television (Cases C 262/02, *Commission v. France*, and C 429/02, *Bacardi France v. TF1, Groupe Jean-Claude Darmon and Girosport*), the Court held that the member states could justify legislation regulating the alcohol industry in order to protect public health and safety (Kurzer, 1998). In other cases, however, the court has ruled that the means used to regulate the alcohol market were not proportionate to attain the objective of protecting young persons from the harmful effects of alcohol. Under Swedish law, for example, private individuals must apply to the Swedish retail monopoly, called Systembolaget, to import any alcoholic beverages not available through the state-run stores. In Case C-170/04, *Klas Rosengren and Others v. Riksaklagaren* (2007), the court held that the prohibition was a quantitative restriction on the free movement of goods that could not be justified on public health grounds, since Sweden had failed to demonstrate that the process was necessary to prevent underage drinkers from gaining access to alcohol. Therefore the ECJ closely analyzes the restriction in each case to determine whether it is proportionate to the stated public interest goal, such as public health.

European Public Health Alliance http://www.epha.org	EPHA is an international non-profit association composed of not-for-profit organizations working on all aspects of public health. EPHA's mission is to promote and protect the health of all people living in Europe and to advocate for greater participation of citizens in health-related policy making at the European level.
European Network for Smoking Prevention http://www.ensp.org	ENSP's mission is to develop a strategy for coordinated action among organizations active in tobacco control in Europe by sharing information and experience and through coordinated activities and joint projects. ENSP aims to create greater coherence among smoking prevention activities and to promote comprehensive tobacco control policies at both national and European levels.
European Alliance on Drug Policy and Practice http://www.eadpp.eu	The mission of the EADPP is to create a channel for dialogue between the European Institutions and key stakeholders involved in prevention, treatment, care and (community) empowerment in the drug field; to influence the development of policy on reducing drug related harm; to encourage bottom up ideas and models of good practice from local or national level to European level; and to communicate European drug strategies and action plans back to national and local level.
EUROCARE European Alliance for Alcohol Policy http://eurocare.org	EUROCARE was formed in 1990 as an alliance of voluntary and non-governmental organizations representing a diversity of views and cultural attitudes and concerned with the impact of the European Union on alcohol policy in Member States. Member organizations are involved in the provision of information to the public; education and training of voluntary and professional community care workers; the provision of workplace and school based programs; counseling services, residential support and alcohol-free clubs for problem drinkers; and research and advocacy institutes.

Table 3. Relevant European non-governmental health organizations. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The increased attention paid to alcohol-related harms encouraged a belated discussion of the public health aspects of underage and excessive alcohol consumption. In 2001 a Council Recommendation titled "Community Strategy to Reduce Alcohol Related Harm" recognized that alcohol was a key health determinant and invited the Commission to develop a comprehensive strategy to reduce the negative health impacts of alcohol. Accordingly, the Commission began public consultations and solicited reports to analyze the problem. One study estimated the economic cost of alcohol-attributable crime to be 33 billion euros in 2003. Alcohol is also responsible for about 195,000 deaths in the EU each year (Anderson & Baumberg, 2006). Based on these reports and public consultations the Commission published its 2006 Communication, the *EU Strategy to Support Member States in Reducing Alcohol-Related Harm*. The strategy focuses on five priority themes: (1) protect young people, children, and the unborn child; (2) reduce injuries and deaths from alcohol-related traffic accidents; (3) prevent alcohol-related harm among adults; (4) reduce the negative impact of alcohol in the workplace (such as absenteeism, drinking on the job, and health issues); and (5) develop, support, and maintain a common evidence base. The Commission defined its role as: (1) to inform, educate, and raise awareness about the major public health concerns regarding alcohol consumption, and to cooperate with member states in addressing these; (2) to initiate action at the EU level through public health programs; and (3) to support and help coordinate national actions by identifying and disseminating good practices across the EU.

In June 2007, the European Alcohol and Health Forum was established to facilitate the implementation of the 2006 Communication. Forum members include European umbrella organizations capable of playing an active role in reducing alcohol-related harm in the EU. These groups will engage in concrete and verifiable commitments to reach this goal. The forum meets twice a year and focuses on concrete actions to protect children and young people and prevent irresponsible commercial alcohol communication and sales. It has also created task forces to focus on youth-specific aspects of alcohol consumption and on alcohol marketing.

ILLICIT DRUGS

Due to the local nature of illicit drug use and related crime, there is a wide variation in national legislation, policies, and expenditures within the European Community. There are no directives specifically regulating drugs from a public health perspective, but the EU coordinates information gathering and dissemination, as well as the identification and sharing of best practices for drug treatment and control. In 2003 the Council of the European Union released its *Recommendation on the Prevention and Reduction of Health Related*

Tobacco	
Tobacco Products Directive 2001/37/EC	Directive on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco products
Tobacco Advertising Directive 2003/33/EC	Directive on the approximation of the laws, regulations and administrative provisions of the Member States relating to the advertising and sponsorship of tobacco products
Commission Decision 2003/641/ec	Commission Decision on the use of color photographs or other illustrations as health warnings on tobacco packages
Council Recommendation 2003/54/EC	Council Recommendation on the prevention of smoking and on initiatives to improve tobacco control
Council Decision 2004/513/EC	Council Decision concerning the conclusion of the WHO Framework Convention on tobacco control
Commission Green Paper January 2007	Towards a Europe free from tobacco smoke: policy options at EU level
Alcohol	
Council Recommendation 2001/458/EC	Council Recommendation on the drinking of alcohol by young people, in particular children and adolescents
Commission Communication COM(2006) 625	Commission Communication on an EU strategy to support Member States in reducing alcohol related harm
Drugs	
Council Recommendation 2003/488/EC	Council Recommendation on the prevention and reduction of health-related harm associated with drug dependence
Commission Green Paper COM(2006) 316	The Role of Civil Society in Drugs Policy in the EU

Table 4. Key European Union public health legislation. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Harm Associated with Drug Dependence. This document focused on the need for member states to actively address drug-related health issues at the state and local level.

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) compiles and reports data regarding the problem of illicit drugs in the EU, but it has no regulatory authority. EMCDDA helps to develop national monitoring systems based on common methodologies and standards, thus providing an evidence base for policymakers at the national and European levels. Generally, cannabis use seems to have leveled off in the first decade of the twenty-first century, while cocaine use is on an upward trend. Interventions in the 1990s were effective at controlling the spread of HIV among infected drug users in most of Europe, but HIV is still prevalent, especially in the Baltic states. Hepatitis C rates are high among injecting populations, and studies have shown that young injectors continue to acquire the disease relatively quickly, making early intervention crucial. The downward trend in drug-related deaths also seems to have leveled off, apparently because of an increase in overdoses by young users (EMCDDA, 2007).

The comparative information generated by the EMCDDA contributed to the development and implementation of the EU Drugs Strategy for 2005–2012, which was outlined in a 2004 Communication. The strategy is intended to reduce both the demand and supply of drugs, with a budget of 21,350,000 euros (US $33,551,000) (CEU, 2004). Due to the EU's limited competence to work in this field, the strategy focuses primarily on research, information dissemination, and evaluation. At the EU level, the Horizontal Working Party on Drugs, a coordinating committee within the Council, was established to monitor the implementation of the actions set out in the EU Action Plans on Drugs, and to coordinate other Council working groups dealing with drug-related issues. (Two action plans were announced, one covering the period 2005–2008, and the other covering 2009–2012.)

Demand-side strategies focus on the development and implementation of integrated and comprehensive knowledge-based demand reduction systems, including treatment, harm reduction, and rehabilitation and social integration. Supply-side strategies involve several branches of EU institutions. EU legislation provides a framework for the

control of trade in the chemical precursors for drugs, both within the Community and in other countries. This legislation is enforced through the Commission's Environment Directorate-General (DG). With regard to money laundering, the Council set out a number of measures to prevent the laundering of drugs proceeds in the 2005 *Third Directive on Money Laundering*. The DG for Justice and Home Affairs, meanwhile, has encouraged cooperation between police, customs, and judicial authorities. Finally, in the area of external relations, the EU is taking international action through a combination of political initiatives, including the action plans, dialogue with various regions of the world, and assistance through development programs to third country sources of drug supply.

In June 2006 the Commission published its "Green Paper on the Role of Civil Society in Drugs Policy in the European Union." At the same time, The DG for Justice and Home Affairs organized the Civil Society Forum for Drugs, and it called for interested civil society organizations to formally express their interest in taking part in such a forum. The December 2007 meeting of the forum addressed current issues arising from the first EU Action Plan on Drugs, and a Progress Review was carried out by the Commission. The forum provides a channel for exchanging views, ideas, and information between the Commission and civil society organizations, and it provides for civil society input on the policy development and reflection process at the European level. The April 2007 *Commission Report on the Implementation of the 2003 Recommendation on the Prevention and Reduction of Health-Related Harm Associated with Drug Dependence* provides that the current status of implementation across EU will be used as a baseline for comparison with future studies. The Commission proposes that the action plan for 2009–2012 include a Council recommendation on reduction of drug-related harm in prisons, as well as a report on drug-treatment programs designed to encourage an exchange of good practice information.

Selected departments and initiatives

DG Health and Consumer Protection, SANCO	Responsible for public health, consumer policy, food safety, animal health http://ec.europa.eu/dgs/health_consumer/index_en.htm
Commission's Public Health Strategy	Includes links to information, documents, and programs on the public health http://ec.europa.eu/health/index_en.htm
Health EU	Includes data and information on Public Health initiatives and programs at EU level http://ec.europa.eu/health-eu/health_in_the_eu/index_en.htm
DG Justice Freedom and Security	Illegal Drugs; Immigration policy and integration, protection of personal data concerning health http://ec.europa.eu/justice_home/web/policy/drugs/web_drugs_en.htm
DG Employment Social Affairs and Equal Opportunities	Safety and Health at work; coordination of Social security schemes including the EHIC card; access of people with disabilities to social health services; Europe Social Fund http://ec.europa.eu/employment_social/health_safety/index_en.htm
DG Agriculture and Rural Development	Nutritional aspects in promotional campaigns for EU agricultural products, information campaigns on smoking http://ec.europa.eu/agriculture/markets/tobacco/index_en.htm
Anti-Fraud Office OLAF	Illicit trade in tobacco products http://ec.europa.eu/anti_fraud/index_en.html

Table 5. European Commission, selected departments and agencies. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

CONCLUSION

EU institutions have become increasingly active in addressing public health risks and investing in programs to reduce the harm caused by tobacco, alcohol, and illicit drugs. EU policies regulating these substances are a complex web of binding legislation and nonbinding recommendations. Member States are under increasing pressure, both politically and financially, to reduce the burden caused by unhealthy lifestyles that risk public health. Those responsible for designing and implementing EU policies in these fields include supranational, national, and local government organizations, as well as various nongovernmental organizations, such as the European Public Health Alliance, the European Network for Smoking Prevention, the European Alliance on Drug Policy and Practice, and EUROCARE (European Alliance for Alcohol Policy). The Commission's white paper "Together for Health: A Strategic Approach for the EU 2008–2013" identifies drugs, alcohol, and tobacco as key health determinants that must be addressed to realize the objective of fostering good

health in an aging population. The strategy sets out implementation mechanisms for cooperation between partners, reinforcing health in all policies, and increasing understanding about health issues at the EU level.

The EU has frequently had difficulty balancing economic and social interests. As was mentioned above, for example, the EU simultaneously funds tobacco agricultural subsidies and antismoking campaigns, while large-scale alcohol production and distribution frustrates efforts to reduce harm from underage and excessive alcohol consumption. In addition, many of the funding streams and public health programs have not been adequately evaluated, either for efficiency or effectiveness. Indeed, the EU is still trying to define its role in addressing these issues, and it could take a more proactive role in promoting public health strategies to reduce the ill effects of drugs, alcohol, and tobacco.

See also **Britain; Eastern Europe; Foreign Policy and Drugs, United States; France; Germany; International Drug Supply Systems; Ireland, Republic of; Spain.**

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EXCLUSIONARY RULE. In legal proceedings, the exclusionary rule prohibits the use of any evidence obtained in contravention of the U.S. Constitution. The rule is frequently invoked when government authorities seize evidence in violation of the Fourth Amendment's prohibition against unlawful searches and seizures. Evidence may be illegally obtained when government officials do not have a warrant to search an individual's premises or the warrant is defective. Law enforcement officers may also lack sufficient probable cause to arrest a person. In addition, the courts may invoke the exclusionary rule when they find a violation of an individual's Fifth Amendment right against self-incrimination or a violation of a defendant's Sixth Amendment right to counsel. Courts often refer to evidence obtained in violation of the Fourth, Fifth, or Sixth Amendment as "tainted" or "the fruit of a poisonous tree."

The U.S. Supreme Court established the exclusionary rule in the early 1900s. It applies to all federal courts through the Fourth Amendment and to all state courts through the Due Process Clause of the Fourteenth Amendment. Before the rule was created, any evidence was admissible in a criminal trial if the judge found it relevant. It made no difference how the police had obtained it. In *Weeks v. United States*, 232 U.S. 383, 34 S.Ct. 341, 58 L.Ed. 652 (1914), the Supreme Court barred the use of evidence secured through a warrantless search of a defendant's house by federal agents. However, for almost fifty years the exclusionary rule only applied to federal courts.

The Supreme Court broadened the rule's coverage in *Mapp v. Ohio*, 367 U.S. 643, 81 S.Ct. 1684, 6 L.Ed.2d 1081 (1961). It held that the Due Process Clause of the Fourteenth Amendment requires states to exclude evidence obtained from an unconstitutional search or seizure. The Court has often cited an individual's right to privacy and the deterrence of unreasonable police conduct as the primary reasons for excluding evidence obtained from an unreasonable search and seizure.

A criminal defendant who claims an unreasonable search and seizure is usually allowed to make the claims in a suppression hearing that is conducted before the trial. At this hearing the judge must determine what evidence will be suppressed or excluded from trial.

A number of exceptions to the exclusionary rule have emerged to reduce the effects of the doctrine, such as a police officer's good-faith belief that an otherwise defective warrant is valid, evidence

obtained in hot pursuit, or evidence seized in plain view of the law enforcement officer's sight and reach. There are other exceptions to the exclusionary rule. Evidence seized by private parties is not excluded from trial if the search was not at the direction of law enforcement officers. If a criminal defendant testifies in his or her own defense, illegally seized evidence may be used to discredit the defendant's testimony. Illegally seized evidence can also be used in grand jury proceedings and civil proceedings. However, a grand jury cannot use illegally seized evidence if it was obtained in violation of federal wiretapping statutes.

IMPORTANCE IN DRUG CASES AND ENFORCEMENT

The exclusionary rule prohibits the introduction of constitutionally tainted evidence. The effect of the doctrine has often been the exclusion of evidence that might be used to convict a suspected drug trafficker or abuser. Courts have excluded evidence of drug paraphernalia or supplies illegally seized, admissions obtained by coercion or without notifying the party of the right to remain silent, and evidence obtained in violation of a defendant's Sixth Amendment right to counsel, such as a lineup identification. The Supreme Court has determined that it is preferable to allow a drug trafficker to go free than to permit law enforcement officers to violate a citizen's constitutionally protected rights.

Two recent Supreme Court cases illustrate the polarities in Fourth Amendment exclusionary rule cases. In *Minnesota v. Carter*, 525 U.S. 83, 119 S.Ct. 469, 142 L.Ed.2d 373 (1998), the Court had to balance law enforcement and privacy interests in assessing the reasonableness of a drug search and seizure. The key issue was whether a police officer who looked in an apartment window through a gap in a closed window blind violated the privacy of the drug dealers in the apartment because they had an expectation of privacy that is protected by the Fourth Amendment. The Supreme Court held that the police officer did not violate the Fourth Amendment because the occupants of the apartment did not have an expectation of privacy. Therefore, the drugs that the police officer saw and later seized did not have to be excluded from evidence.

The outcome was much different in *Bond v. U.S.*, 529 U.S. 334, 120 S.Ct. 1462, 146 L.Ed.2d 365 (2000). In this case, the Court ruled that police cannot squeeze the luggage of bus passengers to try to find illegal drugs. The U.S. Border Patrol routinely squeezed carry-on luggage of bus passengers at a permanent Border Patrol checkpoint near the Texas-Mexico border. Border Patrol officers discovered a brick of methamphetamine after feeling the defendant's soft-sided bag. The Supreme Court noted that the Fourth Amendment provides that a person's effects are protected from unreasonable searches and seizures. A traveler's piece of luggage was clearly an effect protected by the amendment. It found that a "bus passenger clearly expects that his bag may be handled. He does not expect that other passengers or bus employees will, as a matter of course, feel the bag in an exploratory manner." Because the agent did manipulate the bag, he violated the Fourth Amendment. In addition, the Court ruled that the defendant's expectation of privacy was reasonable. It distinguished prior rulings that defeated exclusionary rule challenges because they were based on visual inspections, not tactile inspections.

The Supreme Court continued to relax the use of the exclusionary rule in *Hudson v. Michigan*, 547 U.S. 586, 126 S.Ct. 2159, 165 L.Ed.2d 56 (2006). The Court held that the exclusionary rule did not apply when police officers enter a home to execute a search warrant without following the knock-and-announce rule. This rule, which reaches back to medieval England, requires police to announce themselves and give the resident an opportunity to open the door. The Court reasoned that although the exclusionary rule serves to protect the interests of the Fourth Amendment, the purposes behind the knock-and-announce rule did not protect a person's interest in preventing the government from seizing evidence described in a warrant.

The Court also was concerned that there were considerable social costs in applying the exclusionary rule to knock-and-announce cases. Allowing dangerous criminals to go free was one cost; another was the prospect of many criminal defendants claiming a knock-and-announce violation in hopes of suppressing incriminating evidence. Another reason was that police officers would wait

longer than the law required, leading to preventable attacks on officers and the destruction of evidence. Persons who have suffered a knock-and-announce violation could sue the police for damages under federal civil rights laws as a means of deterrence.

See also **Crime and Drugs; Drug Courts; Drug Laws, Prosecution of; Seizures of Drugs.**

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EXPECTANCIES. The concept of *cognitive expectations* was introduced by psychologist Edward Tolman (1932), who later simplified the term to *expectancies* and defined them as cognitive "sets in the nervous system aroused by environmental stimuli" that influence subsequent behavior (1945, p. 165). Formalized by MacCorquodale and Meehl in 1953, and applied to human social behavior by Rotter in 1954, expectancies came to be understood as "stored information," that allows animals and humans to "act appropriately to impending events" (Bolles, 1972, p. 402). By "appropriately" Bolles meant in an "evolutionarily beneficial" manner.

The concept of *expectancy/anticipation/prediction* has emerged independently in increasingly diverse scientific venues (Goldman, 2002; Goldman et al., 2006), demonstrating that the brain may be well characterized as an "anticipatory machine" (Dennett, 1991) that includes "neural networks that match sensory input with learned expectations"; these processes "help explain how humans see, hear, learn, and recognize information" (Grossberg, 1995, p. 438). Venues in which expectancy explanations have emerged include operant and classical conditioning, comparative judgment, models of memory, the neurobiology of animal and human reward and reinforcement, perception of motion, development of language, time perception, brain electrophysiology, music appreciation, visual orienting behavior in early infancy, and social functioning and the neurobiology of interpersonal trust, among others. At more basic levels, Kupfermann and colleagues (2000) refer to similar processes when they say, "homeostatic regulation is often *anticipatory*" (italics added; p. 1007). Adjustment of the homeostatic set point to anticipate repeated stressors has been called *allostasis*, a process implicated in alcohol and drug addiction.

In the clinical domain, expectancy has been related to mood dysfunction, fear, pain reduction, sexual dysfunction, asthma, drug abuse, alcohol abuse and dependence, smoking, placebo and nocebo (psychologically induced illness or even death) effects, psychotherapy, hypnosis, and medicinal effects of drugs, among others.

EXPECTANCY MEASUREMENT

Applied to substance use, expectancies have been most often characterized as individual cognitions, developed via past experience (direct or vicarious) of alcohol/drug use in one's environment, that anticipate affective, cognitive, and behavioral outcomes, thereby encouraging or discouraging alcohol/drug use. Because considerable variation (individual differences) in verbally reported expectancies has been found, the expectancy construct addresses why some substance users engage in drug use above and beyond beneficial outcomes (increased sociability, relaxation) to the point at which adverse outcomes (including death) are possible.

In the substance use arena, the development of expectancy measurement was preceded by *balanced placebo studies* of (primarily) alcohol effects, in which the influence of expectancies was inferred, rather than directly measured. In these studies, participants consumed a beverage that might or might not have contained alcohol but were independently told whether alcohol was present. This framework resulted in four groups: receiving alcohol and expecting alcohol, receiving alcohol and expecting placebo, receiving placebo and expecting alcohol, and receiving placebo and expecting

placebo. Individuals who consumed placebo alcohol often displayed altered behaviors or mood, presumably as a result of expectancy activation. More recent neuroimaging research along the same lines has, in fact, shown that brain regions and neurotransmitters responsible for reward (e.g., dopamine) can be activated in response to substance cues, even in the absence of consumption.

These findings led to the use of psychometrically based instruments that explicitly capture the expectancies only inferred in the earlier balanced placebo designs. Too many instruments of this kind, tapping expectancies associated with a number of different substances, have been developed to list them all here. Examples include the Alcohol Expectancy Questionnaire (AEQ; Brown et al., 1980), the Cocaine and Marijuana Effect Expectancy Questionnaires (CEEQ; MEEQ; Schafer & Brown, 1991), Comprehensive Effects of Alcohol (CEOA; Fromme et al., 1993), the Smoking Consequences Questionnaire (SCQ; Brandon & Baker, 1991), and the Alcohol Expectancy Multi-Axial Assessment (A. E. Max; Goldman & Darkes, 2004). Within error-attenuated structural models, such instruments have accounted for as much as 50 percent of the variance in substance use, both concurrently and prospectively.

A further application of expectancy instruments is the development of models of alcohol expectancies as they are stored in hypothetical memory networks (Rather & Goldman, 1994.) As of 2008, these types of models had yet to be applied to other drug expectancies. These models suggest that more specific expectancies can be located in multidimensional space along dimensions of valence and arousal. Where a particular individual's expectancy profile falls within this space is reliably related to the individual's extent of alcohol use, such that heavier drinkers consistently endorse more positive and arousing effects of alcohol, and lighter drinkers and abstainers endorse more negative effects. Cross validation of these models has come from laboratory-derived cognitive techniques, such as free association.

Expectancies have also been probed in children, via scales such as the Alcohol Expectancy Questionnaire-Adolescent (AEQ-A; Christiansen et al., 1982), Marijuana and Stimulant Effect Expectancy Questionnaires for adolescents (Aarons et al., 2001), and the Memory Model-based Expectancy Questionnaire (MMBEQ; Dunn & Goldman, 1996). These scales have shown expectancies to be present in children before drinking begins (demonstrating that they are not just a byproduct of consumption), and then to maintain a reciprocal relationship with drinking over time, with more positive expectancies leading to more drinking, and more drinking to increased expectancies (Smith et al., 1995). Initially, children endorse more negative expectancies of substance use, primarily before drinking or drug use begins. However, at some point during early adolescence but preceding the onset of substance use, children begin to develop more positive and arousing expectancies with substance use.

IMPLICIT EXPECTANCY MEASUREMENT

Expectancies have been measured using explicit verbal methods and have been addressed using implicit or indirect cognitive approaches such as the Stroop task, free associates, and expectancy priming. That expectancies can be implicit should come as no surprise given that expectancies were originally posited as explanatory devices in animal research, in which explicit verbal measurement of expectancies is obviously impossible. Although indices derived from these cognitive methods typically account for less variance in substance use behaviors than do explicit measures, they provide a window into the multiple pathways of expectancy operation.

For example, during a free associate task in which individuals were asked to quickly complete the sentence "Drinking alcohol makes me . . . ," heavier drinkers first associated arousing effects of drinking (happy), while lighter drinkers first associated sedating effects (sick; Reich & Goldman, 2005a). Heavy drinkers also displayed increased interference during arousing and positive expectancy words on a modified Stroop task, during which they had to name the color of expectancy words after being primed with alcohol and neutral words (Kramer & Goldman, 2003). Lighter drinkers experienced interference during sedating and negative expectancy words. Essentially, heavier drinkers appeared to activate positive and arousing outcomes (and lighter drinkers to activate sedating and negative outcomes) following an alcohol prime. Heavier drinkers also associated alcohol-

related meaning to ambiguous stimuli (e.g., "bar" or "pitcher"), and remembered positive, arousing expectancy words better if the first word on the list was alcohol-related (e.g., "beer" instead of "milk"; Stacy, 1997; Reich & Goldman, 2005b). These studies suggested that individualized implicit cognitive processes might mediate decisions people make about whether and how much to drink.

EXPECTANCIES AND ADDICTION

Expectancies have been related not only to the onset and maintenance of substance use, but also to the development of substance use disorders (SUDs). Drug addiction has been considered "an abnormal set of motivated behaviors" (Cardinal & Everitt, 2004, p. 156), and anticipation of reward plays a central role in motivating behavior. Individuals with the most problematic drug use typically have endorsed the greatest positive expectations of drug use. Expectancies also partially mediate the relationship between antecedents of risk (family history, gender, race, age, and personality variables) and the development of substance use disorders (Goldman et al., 1999).

Children of alcoholics with more positive alcohol expectancies experienced an earlier onset of regular drinking and were more likely to develop alcoholism themselves (Shen et al., 2001), especially if they were male (Ohannessian & Hesselbrock, 2004), impulsive (Finn et al., 2005), or had social anxiety disorder (Ham et al., 2002). Depressed individuals with a history of alcoholism were more likely to endorse more positive expectancies for drug use, rendering them more likely to fail in attempts to curb drug and alcohol use (Currie et al., 2001). These relationships have also been seen at the genetic level, such that alleles encoding enzymes that most efficiently break down alcohol in the body have been shown to contribute to the development of positive and arousing expectancies, which promote problematic drinking behavior (Hahn et al., 2006).

Expectancies also have significantly discriminated heavy drinkers who maintained very high levels of drinking from those who subsequently reduced drinking behavior over time (Greenbaum et al., 2005). In treatment studies, expectancies predicted post-treatment outcomes, such that those with less positive and less arousing expectancies were more likely to recover. Ultimately, expectancy manipulation may have the potential to decrease drinking and encourage SUD recovery.

EXPECTANCY CHALLENGE

The aforementioned balanced placebo studies have shown that behaviors usually attributed to the neurochemical effects of alcohol were instead due to the activation, under appropriate cue conditions, of a drinker's expectancies about the presumed influences of alcohol. In addition, the development of questionnaires assessing alcohol expectancies has revealed that measured alcohol expectancies were directly related to drinking levels. It has thus become reasonable to suppose that disrupting, or challenging, a person's expectancies might decrease both motivation to drink and drinking behavior. Early tests of this supposition were carried out as experiments using limited participant pools. The challenge paradigm involved a group of individuals consuming either alcoholic beverages or placebo drinks in an experience that mimics a typical drinking situation (e.g., a party). Following this experience, participants were challenged to identify who amongst them actually received alcohol. If only two or three drinks had been consumed (maintaining low-to-moderate blood alcohol levels in those that actually consumed alcohol), participants were usually unsuccessful in correctly identifying the drinkers. Many positive and arousing effects of alcohol were then exposed to result from individual alcohol expectations, and not from the pharmacology of alcohol, and subsequent measured expectancies decreased and drinking over several weeks was diminished (Darkes & Goldman, 1993; 1998).

Subsequent alcohol expectancy challenge modifications have been tested, yielding varying results. Such modifications have included vicarious challenges via videotape (Keillor et al., 1999) and purely didactic (lacking the placebo manipulation) challenges (Corbin et al., 2001). The original protocols designed for use and demonstrated effective with college-aged males have also been modified for use with female drinkers (Dunn et al., 2000; Musher-Eizenman & Kulick, 2003), mixed gender groups (Wiers & Kummeling, 2004), for classroom presentation to elementary school children (Cruz & Dunn, 2003) and applied in combination with Brief Motivational Interviewing (BMI; Wood et al., 2007).

Results across this range of modifications have been mixed, with different effects reported across studies and populations, inconsistent changes in drinking (most notably in female attendees), and no apparent increase in the utility of the challenge when combined with brief motivational interviewing. These studies suggest that the experiential disconnection between alcohol consumption and alcohol-related behavior may play a role in reducing placebo effects of alcohol and could change substance use behavior.

Expectancies were originally identified as the mechanism by which organisms interact with their environment and behave in evolutionarily advantageous ways. It has become increasingly evident that the expectancy construct is vital to the understanding of behavioral phenomena across many disciplines, including addiction. The development of substance use expectancy measures (both explicit and implicit) have revealed that expectancies contribute to the onset and maintenance of substance use behavior and to some extent mediate the relationship between risk and SUDs. Furthermore, organized challenges (or disruptions) to more positive expectancies (via expectancy challenge paradigms) have reduced substance use behavior, with future potential for use as clinical interventions targeting problematic substance use behavior. The expectancy concept does not apply to one circumscribed domain. Consequently, to move forward in expectancy research, conscious efforts must be made to identify common expectancy pathways across multiple domains both in and outside the field of addiction and psychology.

See also **Coping and Drug Use; Models of Alcoholism and Drug Abuse; Prevention; Treatment; Women and Substance Abuse.**

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FAMILIES AND DRUG USE. Despite increased primary school-based prevention efforts throughout the 1990s and the 2000s, alcohol and drug use among teens has remained stable, with a small percentage of teens (3.5%) developing alcohol dependence (Young et al., 2002). These individuals are at high risk of experiencing chronic substance-abuse-related problems into adulthood. Yet only about 16 percent of youth in need receive treatment for alcohol and drug problems, according to the Substance Abuse and Mental Health Services Administration (1996), and those that receive standard treatment in the community relapse at high rates within the year following treatment (Cornelius et al., 2003). Thus, more effective interventions for adolescent substance misuse are needed.

FAMILY FACTORS IN SUBSTANCE ABUSE

Substance abuse has multiple interacting precipitators, and family factors play a central role both in early substance use and its progression. A range of family risk factors correlate consistently with adolescent substance abuse, including poor family functioning, parent and sibling substance use, ineffective parental monitoring, family conflict, and low levels of family support. Family factors are also among the strongest protective influences against drug taking. Parents protect teens from early drug and alcohol initiation and abuse by setting clear standards against use and by setting limits. Family factors also exert an important mediational role in explaining other risk factors for drinking and drug use. While peers have a direct effect on teen substance abuse, parents mediate these influences by monitoring and maintaining close relationships with their adolescents. Family factors appear to operate both directly and indirectly to predict teen substance use, indicating the need for effective family-based interventions for alcohol and drug problems.

Several clinical trials have provided strong and consistent empirical support for the comparative efficacy of family-based interventions in reducing levels of adolescent drug use and increasing adaptive functioning (Waldron & Turner, 2008). Family-based interventions demonstrate considerable effectiveness in reducing teen drug use compared to individual therapy, adolescent group therapy, and family psychoeducational counseling. The superior posttreatment effects of family-oriented treatments have been retained for up to 12 months after termination (Liddle et al., 2002), and in one case for up to four years posttreatment (Henggeler et al., 2006). Furthermore, family-focused treatments improve family functioning, school performance, comorbid psychiatric symptomatology, and delinquency.

FAMILY-BASED INTERVENTION OUTCOMES

Progress has been made in developing treatments for adolescent alcohol abuse and outlining the critical factors and processes in alcohol recovery and relapse among youth. However, in the first year following standard community-based treatment, more than half of teens relapse (Maisto et al., 2001), and over time (from 1 to 8 years) alcohol

use rises steadily in each consecutive year following treatment (Tapert et al., 2003). Few empirically developed models for adolescent alcohol abuse exist, and little is known about the intervention features that impact adolescent alcohol use following treatment. However, with new evidence about the multiple contributing factors to alcohol risk and protection, there is consensus that interventions for alcohol use disorders must simultaneously target the multiple factors and systems that create and maintain problems. Family-based approaches have potential in this regard, yet their promise with adolescent alcohol abusers has rarely been tested, and they certainly have yet to be fully realized.

There is some evidence that family-based interventions reduce alcohol use and related problems among teens. For instance, the Purdue Brief Family Therapy model significantly reduced adolescent alcohol use in fewer sessions than drug education and individual treatment as usual (Trepper et al., 1993), while behavioral family therapy was more effective than supportive counseling in reducing adolescent alcohol use up to nine months following treatment (Azrin et al., 1996).

FAMILY-BASED INTERVENTION FOR ADOLESCENT SUBSTANCE ABUSE

Efforts to intervene with youth at risk for substance use problems incorporate knowledge of both the developmental pathways to drug and alcohol use disorders and the multiple risk factors for these disorders. Family-based therapies target the major risk factors, established through longitudinal and cross-sectional studies, known to be the precursors to substance abuse in adolescence and young adulthood.

An example of one of the new generation of family-based therapies is multidimensional family therapy (MDFT). Other family-based treatments have also been developed that show evidence of positive outcomes, such as multisystemic therapy, functional family therapy, and brief strategic family therapy (see Austin, Macgowan, & Wagner, 2005; Vaughn & Howard, 2004; Waldron & Turner, 2008). The focus here is on MDFT in order to illustrate with some detail the main features of one of these models. The MDFT treatment system assesses and intervenes in four main areas: adolescent, parent, family, and extrafamilial systems. With adolescents, therapists seeks to transform a substance-using lifestyle into a developmentally normative one with improved functioning across various domains (e.g., peers, identity, school, and family relationships). Goals for parents include increasing parental commitment and improving parent-teen communication and parenting practices such as monitoring. In family sessions, MDFT therapists promote supportive and effective communication among family members.

With adolescent alcohol problems, three areas deserve particular attention: alcohol expectancies, parental substance abuse, and family-based relapse prevention and aftercare services.

Alcohol Expectancies. The alcohol expectancies of an adolescent are a strong predictor of problem drinking (Colder et al., 1997). Alcohol expectancies include beliefs about the positive social and emotional effects of alcohol (e.g., appearing more comfortable to others and feeling more relaxed, respectively), as well as beliefs that alcohol is less harmful than it actually is. Adolescents' alcohol expectancies and attitudes connect to the norms families communicate about drinking. Children not only adopt their parents' drinking behaviors, they also adopt the coping strategies and motivations that are modeled by their parents (Ouellette et al., 1999). Thus, interventions to change adolescents' expectancies must also involve a shift in parents' messages and behaviors (Windle, 1996).

MDFT addresses the social cognitive aspects of substance use, the meaning and motivation for substance use, and the development of motivation for abstinence. Addressing expectancies, beliefs, and attitudes about alcohol is consistent with the MDFT therapist's work with teens to examine their motivations for using and to help them become aware of the health-compromising aspects of alcohol use. Individual sessions with the adolescent focus on highlighting discrepancies between stated personal goals or outcomes and current lifestyle choices, including beliefs about alcohol and its consequences. Continued use of substances is acknowledged to be incompatible with a nondrinking lifestyle and the benefits of positive changes, such as doing better in school and having less conflict at home. The pathways to achieve these changes also involve parents and other social

systems. Therapists work with parents to examine their messages and norms about drinking, for example. Individual work with adolescents and parents provides a platform for families to talk together about drinking and help the adolescent develop more realistic beliefs about alcohol as well as new skills to avoid drinking.

Parental Alcoholism. Parental alcoholism is one of the strongest and most consistent family risk factors for teen alcohol problems, and there is an increased risk even when the parent's alcoholism is in remission (DeLucia, Belz, & Chassin, 2001). Parental alcoholism increases young adolescents' risk of alcohol abuse through specific mechanisms that can be addressed in family interventions, such as family conflict and lack of cohesion, decreased monitoring, and alcohol expectancies (Chassin, Curran, Hussong, & Colder, 1996; Hussong, Curran, & Chassin, 1998; Sher, 1994).

Directly and systematically addressing parental alcoholism is part of core parent work in MDFT. MDFT targets the functioning of parents as individual adults, apart from their role as parents or caregivers. Because parenting practices are connected to the parent's functioning, parental substance abuse must be addressed. The therapist motivates the parent to take steps to change their own lives by resuscitating their love and commitment for the child, and therapists link parents' alcohol and substance use to their parenting, highlighting how alcohol use impairs their ability to be consistent, firm, and available to their child.

Family-based Relapse Prevention and Aftercare. The most common precipitators of relapse following treatment are social pressures and negative affect. Protective factors against alcohol relapse include aftercare participation, better alcohol coping skills, and positive supports for recovery (Chung et al., 2004; Latimer et al., 2000). Family functioning has also been found to play a primary role in helping teens achieve and maintain abstinence (Hsieh et al., 1998). These findings underscore the importance of bolstering coping and relapse prevention skills during treatment and providing continued support and aftercare services following treatment.

In MDFT, primary family interventions are aimed at promoting new interactional patterns among family members. Because the family environment is an important context of adolescent functioning, one of the goals of MDFT is to create a new family environment in which the family becomes the therapeutic agent long after the MDFT therapist has completed work with the teen and the parents. Thus, MDFT family sessions use the technique of enactment to elicit and shape discussions of important topics, including alcohol use and ways to cope with drinking urges. These interventions provide opportunities for the therapist to take an active and directive stance toward the prompting of new responses and supportive behaviors from family members. Issues raised in individual sessions are brought into the family meetings, with the encouragement, support, and facilitation of the therapist.

A complementary component of work that helps to maintain the teen's recovery during and following treatment is in the extrafamilial realm. MDFT therapists aim to improve the parents' and adolescent's functioning relative to influential extrafamilial social systems, and also to promote the teen's involvement in prosocial activities. Added support during and following treatment is also facilitated by encouraging adolescents' participation in teen-focused Alcohol Anonymous (AA) meetings. Attendance at AA and other 12-step meetings has been shown to increase motivation for abstinence and predict better outcomes for youths in the three months following treatment (Kelly, Myers, & Brown, 2002). Multiple-systems oriented approaches such as MDFT have the advantage of addressing and providing coordinated comprehensive interventions with intrapersonal, social, familial, and extrafamilial relapse risk factors.

CONCLUSIONS

Experts recommend further development and application of family-based interventions that are comprehensive and multisystemic in scope (see Brannigan et al., 2004). A new wave of treatments based on the family therapy tradition have been created and developed in funded clinical research contexts, and these are increasingly available for dissemination in a wide variety of clinical settings. Variations of these approaches have been designed to more effectively target the needs of different clinical samples, such as adolescent girls, teens from different cultural groups, or those involved in

juvenile-justice settings. The mechanisms by which these therapies achieve their effects have also been investigated (Diamond et al., 2000). This research has fed back into the treatment-development work of the models (Jackson-Gilfort et al., 2001) and helped improve the training and supervision of these science-supported therapies.

While it is known that families and drug use are linked, it is too simplistic and narrow a frame to think of family problems as causing drug use. Indeed, research does not support this notion of causation. It is more correct to say that family functioning is one of several factors that not only creates the conditions in which drug taking can begin, but also represents an important developmental arena that must be taken into account in drug treatment. Previous generations of theorizing and treatment development have either left families out of the recovery equation or blamed families unduly for being the cause of an individual's addiction. Numerous influential policy reports, practice guidelines, and research reviews now conclude that families must be included in the treatment of drug-using teens. Today's family-based therapies have a more enlightened clinical perspective, considerable empirical evidence, and a new family-friendly technology with which to engage and retain parents and teens, through nonblaming and nonpunitive means, in effective treatments.

See also **Adolescents and Drug Use; African Americans, Ethnic and Cultural Factors Relevant to Treatment for; Alcoholics Anonymous (AA); Codependence; Conduct Disorder and Drug Use; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Treatment, Behavioral Approaches to: Couples and Family Therapy; Treatment, Specialty Approaches to: Adolescents.**

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HOWARD A. LIDDLE

FASHION INDUSTRY, INTERNATIONAL.

Although there is little to indicate that the fashion industry has a higher incidence of drug abuse than other, comparable branches of the entertainment industry, it developed a reputation for narcotic use in the last part of the twentieth century. This tendency reached a crescendo in 1996, when New York fashion photographer Davide Sorrenti died from a small dose of heroin. Sorrenti suffered from a rare blood disorder called Cooley's anemia or thalassemia, which explained his susceptibility to even small quantities of the drug; but because he was one of a group of photographers whose work had been dubbed *Heroin Chic* by the press, his death brought wide notoriety to the use and the alleged glorification of drugs in the fashion industry. Within the week, U.S. President Bill Clinton declared that "the glorification of heroin is not creative, it's destructive . . . It's not beautiful, it is ugly. . . . This is not about art, it's about life and death" (*New York Times*, 1997, p. A22).

Clinton's speech resonated across the international fashion world and the industry responded almost immediately by promoting a new, healthier image. Nonetheless, when the model Kate Moss was secretly photographed taking cocaine at a party in September 2005, the British tabloids dubbed her "Cocaine Kate" (Stephen Moyes, *"Cocaine Kate,"* Daily Mirror, May 2005) and, a few months later, called her a "Cocaine Fiend" (Clodagh Hartley, "Kate on Coke at Mandela's," the *Sun*, March 2006). Clearly, the perceived association of fashion and drugs did not die out with the vogue for Heroin Chic at the end of the twentieth century.

VICTORIAN DRUG–USE IMAGERY

The association of drugs with fashion has roots that stretch well beyond the furor of the 1990s. One might begin with Elizabeth Siddal (1829–1862), model and muse of the mid-nineteenth-century Pre-Raphaelite Brotherhood of English painters (Yaeger, 2007). Siddal appeared in many of their paintings, perhaps most famously as the model for John Everett Millais's *Ophelia* (1851–1852). Siddal's depiction, especially in paintings by her eventual husband, Dante Gabriel Rosetti, shows her as young, strikingly beautiful, and somehow longing for things just beyond her grasp, beyond the frame's edge. Siddal's painted image figured youth, beauty, and tragically unfulfilled desire, associations that her 1862 death by laudanum overdose did nothing to diminish. Her demise resonated with the romanticized sense of drug use popularized in Thomas DeQuincey's *Confessions of an English Opium Eater* (1822). DeQuincey's memoir suggested that opium use (the opium and alcohol mixture called laudanum in DeQuincey's case) might offer an intellectual escape from the chains of Western reasoning, opening a path to a philosophical truth that was grander and more exotic than that which he found without the stimulus of drugs. Siddal's image conveyed a longing for a (usually medieval) world that was exotic and pure, one that could replace the industrial reality of mid-nineteenth-century England. Her painted image thus suggested youth, fragility, romantic longing for another, impossible world—all themes that would re-emerge in fashion photography of the late twentieth century.

DRUGS AND BODY IMAGE

Drugs and the fashion industry became closely linked as thinness became an important marker of female beauty. Its opposite, that is, obesity, is implicated in at least two of the seven deadly sins, sloth and gluttony, but any historical examination of western representations of beauty show that the interpretation of what counts as obese has been in constant flux. Obesity, however, is not only an aesthetic issue. It was increasingly treated as a medical condition throughout the twentieth century, according to Thomas C. Shevory (2000). Though the relationship between weight and health remained controversial in the early years of the twenty-first century, the negative health consequences of thinness, at least initially, received much less attention than did those of obesity. Being thin in the 1950s was commonly achieved with diet pills, which was particularly the case beginning in the 1950s, when physicians began to prescribe amphetamines, the first truly effective appetite suppressants, to patients whose goal was to reduce weight. As thinness became increasingly fashionable, those in the

competitive world of fashion modeling soon realized the career-enhancing benefits of effective diet pills. Historian David Courtwright reports that the fashion model Jean Dawnay described her 1950s New York colleagues as living on Benzedrine, Dexedrine, and black coffee. She declared, "their incredible thinness staggered me" (Courtright, 2002, p. 109). Diet pills thus ensured that after the 1950s, fashion models, photographers, and those connected with them would be no strangers to drug use.

At the same time that diet pills were gaining a hold in the fashion industry, a visual discourse of narcotic addiction was being assembled in popular culture and also in law enforcement circles. The Federal Bureau of Narcotics (FBN), established in 1930, was headed by Harry J. Anslinger, who established harsh drug restrictions central to what Courtwright calls the "Classic Era" of anti-narcotic policy—a period when drug enforcement was simple, consistent, and rigid (2002, p. 3). The tone set within the FBN underlay the widespread production and dissemination of images intended to terrify the public—especially young people—in hopes of deterring them from using drugs. The images also played a large role in the popular culture of the mid-twentieth century. The demonization of drugs was also visible in films such as Louis Gasnier's 1936 *Ask Your Children* (more commonly known as *Reefer Madness*). Though part of a somewhat disreputable, exploitative genre, visions of "sex-crazed drug fiends" like those in Gasnier's film were the visual logic of the classic era of narcotic control (Newman, 1996, p. 509).

One consequence of the strong antidrug stance of the Anslinger years was the identification of drug use with inner-city vice districts and with a cultural underworld.

The most visible members of this urban, largely black population were the entertainers—especially jazz musicians—who worked in popular, big-city cabarets and nightclubs. For some people, the creativity of performers such as Charlie Parker and Billie Holiday became associated with their notorious drug use. The image of the drug addict as a deviant was conflated with this vibrant musical culture, and it acquired seductive appeal. Drug use seemed aligned with rejection of the conservative values and attitudes that the Harry Anslingers of the world hoped to promote. In other words, drug use seemed to signify a "hip" rebellion against an allegedly "square" mainstream culture.

Beat generation writers such as Jack Kerouac, Allen Ginsberg, and William S. Burroughs underscored precisely this alignment. Their texts, especially Kerouac's 1956 *On the Road*, idolized people whom the Beats imagined as being outside the dominant culture. From the Beats it is a very short way to the 1960s counterculture and its youth market. Kerouac, Ginsberg, Burroughs, and Neal Cassady all became influential figures within the 1960s counterculture. They brought drug use to the middle-class suburbs and college campuses of white America. Music, film, and fashion also began to glorify drug use as a fashionable rebelliousness. Edie Sedgwick, for instance, achieved celebrity through her connection with Andy Warhol's notoriously drug-associated studio Factory in the early sixties. As a model, she appeared in magazines such as *Vogue* (1965, 1966) and *Life* (1965). Sedgwick, who had been hospitalized with anorexia nervosa in 1962, appealed with her pronounced thinness.

Nonetheless, her modeling career never really took off, at least partly because "she was identified in the gossip columns with the drug scene" according to *Vogue* senior editor Gloria Schiff (Stein, 1982, p. 308). Other celebrity fashion icons such as Talitha Getty and Marianne Faithfull were similarly identified as drug users, but even the 1971 overdose deaths of Sedgwick and Getty did little to diminish their influence on the look of the era.

Drug use thus played a role in defining both the image and the personality of an array of glamorous, countercultural celebrities of the 1960s. The association persisted through the 1970s and 1980s. Partly it persisted because of the increasingly popular work of documentary photographers such as Larry Clark and Nan Goldin, who drew upon the older visual demonization of drugs and also the hip 1960s celebrity culture. Though none of this work glorifies drug use, its seductive images of hip, attractive, and apparently drugged young people contrast with the negative portraits propagated during the Anslinger years. Images depicting the squalor, physical demands, and loneliness of deviant addicts were here replaced by those of stylish, sophisticated people.

The marketing of this romanticized vision of intoxication, an obsession with thinness, a hip

counterculture and tragic celebrity coalesced in the 1990s photographic phenomenon called Heroin Chic, which cemented the popular association of drugs and the fashion industry at the close of the twentieth century. The work of Clark and Goldin, and their evocation of a fashionable counterculture, was repeatedly cited as a major influence on a generation of young fashion photographers who sought what was understood to be a more authentic depiction of beauty than that embodied by the typically airbrushed, polished images presented in glossy fashion magazines (Kakutani, 1996, p. 16). The style chosen by photographers such as Corinne Day, Terry Richardson, Jürgen Teller, and Mario and Davide Sorrenti came to be known as Heroin Chic, a look that began to appear in British fashion and culture journals such as *The Face* and *I–D* during the early nineties, and also in U.S. publications such as San Francisco's *Detour*. It quickly spread across the international fashion scene. The style was connected to the popularity of Seattle's grunge music scene and what was then trumpeted as the *waif* look among fashion models. Heroin Chic images typically employ extremely thin models whose knotted hair, clammy skin and vacant, darkened eyes suggest a life of excess—a look associated with drug use but also with celebrity glamour. The bad publicity and notoriety that was drawn by Davide Sorrenti's death hastened the industry's move away from the fad but, as continuing controversy and negative attention show, the association of drugs with the fashion industry is a tenacious correlation.

See also **Anorexia; Bulimia Nervosa; Epidemics of Drug Abuse in the United States; Heroin; Media; Movies; Music; Sport, Drugs in International.**

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TIMOTHY A. HICKMAN

FERMENTATION. Fermentation is a natural metabolic process that produces energy by breaking down carbohydrates (such as sugars) in the absence of oxygen. It occurs in many microorganisms (such as yeasts), and the end product can be either ethyl alcohol (ethanol) or lactic acid; energy is typically given off in the form of heat. The chemical reaction of this process was first described in 1810 by the French chemist Joseph Louis Gay-Lussac. Fermentation is important to the production of many foods and beverages, the most popular of which are bread, butter, cheese, beer, and wine.

Fermented foods first occurred naturally, when stored or forgotten caches were found to be altered but edible. In ancient times, wheat and barley were domesticated, farmed, stored, and used to make breads and porridges—some of which fermented and formed brews. Since that time, the process of fermentation has been used worldwide. Industrial means provide huge quantities of fermented foods, as well as alcohol, which is obtained by distillation

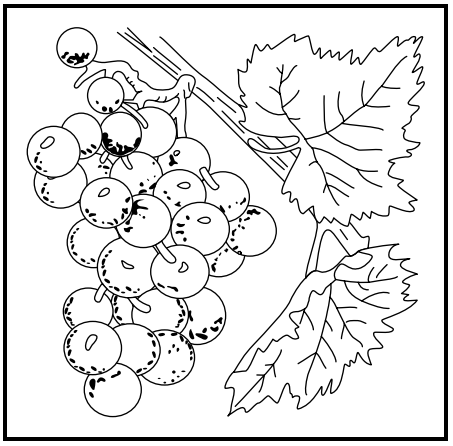

Figure 1. Grapes. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

from fermented juices of fruits, grains, vegetables, and other plants.

See also **Beers and Brews.**

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SCOTT E. LUKAS

FETAL ALCOHOL SYNDROME.

Fetal alcohol syndrome (FAS) is a constellation of behavioral, growth, and facial abnormalities resulting from prenatal alcohol exposure. Diagnosis is made by a specially trained physician and is based on the presence of three criteria: a pattern of distinct and specific facial abnormalities; growth deficiency; and central nervous system (CNS) damage, with or without confirmed maternal alcohol consumption. FAS is at one end of a spectrum, now termed "fetal alcohol spectrum disorders" (FASD). FASD is used as an umbrella term. If a child has some, but not all, of the criteria for FAS, they have one in a spectrum of disorders, covered by the terms ARBD, alcohol-related birth defects, and ARND, alcohol-related neurodevelopmental disorder. Use of the term FAE, fetal alcohol effects, is discouraged because of non-specificity. FASD, short of full FAS, requires documentation of prenatal alcohol exposure.

HISTORY

The term *fetal alcohol syndrome* was first used in 1973 to describe the physical problems seen in the offspring of alcoholic women. There have been admonitions against women drinking during pregnancy for literally thousands of years—at least as interpreted from biblical verses and in the writing of the ancient Greeks. The physical and social implications of women drinking during pregnancy first became highly noticeable during the gin epidemic of the 1750s. At that time, gin became a cheap and easily accessible beverage among low-income women. It was noted that there was a correlation between women who were consuming large amounts of gin and problems among their offspring.

A formal study was conducted in the 1890s by William Sullivan, a physician in England. He identified the offspring of 120 female "drunkards" in the Liverpool jail and compared them to the children of their non-drinking female relatives. From this study, Sullivan noted a perinatal mortality rate that was two and one-half times higher in the offspring of the female alcoholics.

In 1968, Paul Lemoine published a study on the children of female alcoholics in a French medical journal. This article did not receive much attention until the landmark articles published in the *Lancet* by Jones, Smith, Ulleland, and Streissguth in 1973, in which the term *fetal alcohol syndrome* (FAS) was first used. Since 1973, about twenty thousand articles have been published detailing the effects of prenatal alcohol exposure from birth through middle age. In the early twenty-first century it has been commonly accepted that alcohol is a powerful teratogen (causative agent in fetal malformations) with lifelong consequences and that the severity of effects is associated with the amount and pattern of drinking. In particular, children who were exposed in utero to one or more drinks per day or to binge-like exposure (five or more drinks per occasion) tend to show adverse effects. These effects cannot be attributed to alcohol with certainty at lower levels of exposure, but there is strong evidence of differing susceptibility/vulnerability, so it is reasonable to advise women not to drink at all during pregnancy.

DISTRIBUTION

The prevalence of FAS ranges widely from community to community and is determined by the number of women consuming alcohol in any particular community. Every year in the United States, 500,000 women report drinking alcohol during pregnancy, with nearly one in five of those admitting to binge drinking. These statistics translate into a prevalence rate of nearly 13 percent for any consumption, and 6 percent for frequent and binge drinking. As of 2008, FAS was thought to be the leading cause of mental retardation in the United States, surpassing Down syndrome and spina bifida. It is estimated that approximately 1 to 4.8 of every 1,000 children born in the United States has FAS, with as many as 9.1 per 1000 (or nearly 1 in 100) born with FASD. However, few prevalence studies have been conducted as of 2008, and experts have different views as to the accuracy of the prevalence figures available. Additionally, prevalence rates vary widely by region and community, as well as by surveillance methodology. Some studies from the Centers for Disease Control and Prevention (CDC) suggest that drinking during pregnancy may be increasing despite public-health information designed to prevent FAS.

PHYSICAL EFFECTS

Drinking alcohol during pregnancy produces different effects, depending on the amount and when the alcohol is consumed. During the first trimester, there is a chance of major physical abnormalities (ARBDs) and CNS damage. During the first and second trimester, alcohol consumption leads to an increased rate of spontaneous abortion and CNS damage, as well as more subtle physical abnormalities. During the third trimester, alcohol consumption can lead to pre- and postnatal growth restriction and CNS damage.

Three major criteria must be met for a diagnosis of FAS. The common facial abnormalities include short palpebral (eye-slit) fissures; a long smooth philtrum (upper lip groove); and thin upper lip. Other common physical problems associated with prenatal alcohol use are cardiac (heart) malformations and defects; pectus excavatum (hollow at the lower part of the chest due to backward displacement of xiphoid cartilage); clinodactyly and camptodactyly (permanent curving or deflection of one or more fingers); fusion of the radius and ulna at the elbow; scoliosis (lateral curvature of the spine); kidney malformations; and cleft lip and palate. Indeed, a large range of anatomic abnormalities in almost all body systems have been reported to be associated with prenatal alcohol exposure.

Growth deficiency in FAS is specifically noted in three parameters: height, weight, and head circumference. At birth, children with FAS and FASD tend to be small for gestational age with deficits in all three parameters, though deficiencies in all are not required for diagnosis. In addition, while some growth catch-up has been described, by puberty the vast majority of children with FAS/FASD still have growth retardation; they are generally short and thin. Significant changes in weight are noted as females enter puberty; although the growth deficiency remains in height and head circumference across the lifespan, females frequently gain weight and are plump. Males seem to remain comparatively short and slender until their late twenties or thirties.

CNS damage is frequently manifested in cognitive and memory deficits, sleep disturbances, developmental delays, hyperactivity/distractibility, a short attention span, an inability to understand cause and effect, lower levels of academic achievement, impulsivity, and difficulty in abstract thinking. The difficulties noted in infancy and early childhood are often precursors to later psychosocial deficits.

PSYCHOSOCIAL AND EDUCATIONAL ISSUES

Based mostly on caretaker experience and clinical observation (rather than clinical studies), the following describe the development patterns in FAS individuals.

Birth to Age Five Years. Diagnosis of FAS/FASD is possible at birth, but many physicians are either not trained to identify the characteristics or do not consider the possibility. Post-natal behavioral manifestations of FAS/FASD include the following: poor habituation, an exaggerated startle response, poor sleep/wake cycle, poor sucking response, and hyperactivity. Failure to thrive, alcohol withdrawal, and cardiac difficulties are medical concerns sometimes noted in those born with FAS. Also, developmental delays in walking, talking, and toilet training may be observed. Concerns such as hyperactivity, irritability, difficulty in following

directions, and the inability to adapt to changes are commonly reported. The damage done to the brain by the prenatal alcohol exposure makes it problematic for children with FAS to learn in a timely and consistent fashion. The more abstract the task, the more apparent this learning gap becomes, particularly in adolescence and adulthood.

Recommended interventions before the age of five focus on the family as well as the child. Children with FAS/FASD are sometimes removed from the care of the biological mother owing to abuse, neglect, and/or maternal death. Newborns and infants with FAS/FASD often have trouble feeding; when this difficulty is coupled with a mother who may be deeply involved in substance abuse and not attentive to the needs of her infant, it can lead to medical crises. It may be necessary to provide the following services and interventions:

- Health and medical monitoring
- Safe, stable, structured residential placement with services provided to the mother, father, patient, and other family members, such as substance-abuse treatment and parenting training
- Directions given to the caregivers in a simple, concrete fashion, one at a time; directions given to the child in similar fashion
- Adaptation of the external environment to fit the child's ability to handle stimulation
- Setting by caregivers of appropriate goals and expectations for the child
- Respite care and ongoing support for caregivers

Ages Six to Eleven Years. Some of the problems noted earlier, primarily health issues, become less severe as others become more severe, with greater implications for negative social functioning. Hyperactivity, impulsivity, memory deficits, and inappropriate sexual behavior may emerge, as may difficulty predicting and/or understanding the consequences of behavior, difficulties in abstracting abilities, and poor comprehension of social rules and expectations. These are all common among children with FAS/FASD. Children with FAS/FASD may show decreasing ability to function in school as they get older. The abstracting deficits become more apparent when the child reaches the third and fourth grades and is expected to perform multiplication and division. Suggested interventions at this stage include the following:

- Safe, stable, structured residential placement
- Establishment of clear and reasonable expectations, goals, limits, and boundaries
- Consistent structuring of leisure time and activities
- Education of parents, caregivers, and the patient regarding age-appropriate sexual and social development
- Appropriate educational placement that focuses on an activity-based curriculum, development of communication skills, development of appropriate behavior, and basic academic skills embedded with functional skills, in a structured environment, in which competing stimuli are avoided

Ages Twelve to Seventeen Years. Children with FAS/FASD have the same emotional needs as others do at this age, but adolescents with FAS/FASD may also exhibit cognitive deficits, impulsivity, faulty logic, low motivation, lying, stealing, depression, suicidal thoughts and attempts, and significant limitations in their adaptive behavior skills. Social deficits include financial/sexual exploitation and substance abuse. It is frequently difficult for people with FAS/FASD to articulate their feelings and needs, which typically occurs as these individuals reach their intellectual and academic ceiling.

Despite these problems and deficits, adolescents with FAS/FASD should be treated age appropriately within the limits of their developmental ability. The following are some interventions that may help them reach their social, emotional, and adaptive potential:

- Changing the focus from academic to vocational and daily-living skills training
- Structuring of leisure time and activities, such as involvement in organized sports and social activities
- Educating patients, parents, and caregivers regarding sexual development and the need for birth control or protection against sexual exploitation and sexually transmitted diseases (STDs)
- Planning for future vocational training and placements, financial needs, and residential placement
- Increasing responsibility based on the patient's skills, abilities, and interests

Ages Eighteen through Adulthood. The problems, deficits, and difficulties seen prior to the age of eighteen are precursors to those seen in early adulthood and middle age. An additional problem experienced by people with FAS/FASD is the increased expectations placed on them by others. Not only can people with FAS often not meet these expectations but their impulsivity and poor judgment have more serious consequences than during their younger years. Issues such as poor comprehension of social rules and expectations, aggressive and unpredictable behavior, and depression coupled with impulsivity may lead to suicide attempts, antisocial behavior, hospitalization, and/or incarceration. Many can benefit from structured assisted living arrangements.

Other concerns noted in adults with FAS/FASD include social isolation and withdrawal, difficulties in finding and sustaining employment, poor financial management, problems accessing and paying for medical treatment or child care, and a need for help with social/sexual exploitation and unwanted pregnancy. The hyperactivity and distractibility seen in small children with FAS/FASD manifest in the adult's not being able to learn job skills or meet the requirements of many jobs. The following list contains suggested ways to help adults with FAS/FASD and their families deal with problematic issues in a productive fashion:

- A guardianship for or assistance with finances
- Residential placements or community housing to help ensure physical safety while allowing them to live as independently as possible
- Support for medical care, along with birth control planning
- Child-care and parenting classes, as needed
- Education for others about FAS/FASD, including its limitations and skills, to foster acceptance
- Long-term residential/vocational/psychosocial support for patient and/or caregivers

PREVENTION

The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics recommend alcohol abstinence for both pregnant and pre-conception women because no safe threshold for consumption has been identified, and there is evidence of varying susceptibility/vulnerability to the effects of prenatal alcohol exposure. Prenatal practitioners are advised to question all women of reproductive age, and all pregnant women at their first prenatal visit about current and past alcohol use and to use a formal screen for risk-drinking, such as the T-ACE. Questioning again later in pregnancy is also recommended. For women identified as being at risk, intervention is indicated. For most pregnant women, a brief in-office intervention may be all that is needed to reduce the risk of an alcohol-exposed pregnancy. Brief interventions are evidence-based, low-cost, time-efficient, and effective self-help treatments involving counseling that can be delivered by health professionals who are not specialists in the treatment of alcohol use or dependence. Two randomized clinical trials and several other studies have shown that brief interventions, delivered as part of prenatal care, can significantly reduce rates of pregnancy drinking and consequent FAS/FASD neonates. However, for women with exceptionally high rates of consumption or who are diagnosed as alcoholics, more intensive intervention along with referral to specialized treatment programs is recommended.

FAS/FASD is a preventable birth defect; however, once it exists it has lifelong consequences. Special programs involving planning for the future vocational, educational, and residential needs of affected individuals should be implemented as early in childhood as possible. Education on the harmful effects of alcohol use and assistance for women prior to and during pregnancy is critical to help prevent or at least reduce this significant public health problem.

See also **Alcohol- and Drug-Exposed Infants; Alcohol: History of Drinking in the United States; Attention Deficit Hyperactivity Disorder; Fetus, Effects of Drugs on the; Pregnancy and Drug Dependence.**

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FETUS, EFFECTS OF DRUGS ON THE.

The pregnant substance-abusing or drug-dependent woman subjects her developing infant to a host of problems. When assessing the effects of drugs, whether illicit or appropriately administered (not abused) prescription drugs, on newborn infants (neonates) and young children, two factors must be considered: (a) the duration and concentration of the drug exposure on the developing fetus, and (b) any preexisting medical complications in the mother. These factors are interactive and together will influence, in varying ways, the eventual health, learning challenges, and potential capabilities of the child. Therefore, the long-term outcome of children exposed to drugs during fetal development should be assessed.

As cited by Dr. Nancy Young in her presentation on substance-exposed infants, the 2002 and 2003 Substance Abuse and Mental Health Administration (SAMHSA) Office of Applied Studies National Survey on Drug Use and Health (NSDUH) had a specific focus on substance use among pregnant women. It indicated that the reported incidence of pregnant women using any drug was highest in the first trimester, and decreased steadily thereafter: 7.7 percent of mothers affecting 315,161 infants in the first trimester, 3.2 percent of women affecting 130,976 infants in the second trimester, and 2.3 percent of women affecting 94,139 infants in the third trimester reported using any drugs whatsoever. Similar patterns were found for binge alcohol and alcohol use. For alcohol use the statistics were 19.6 percent of women affecting 802,228 infants in the first

trimester, 6.1 percent of women affecting 249,673 infants in the second, and 4.7 percent of women affecting 192,371 infants in the third trimester of pregnancy. For binge drinking of alcohol the statistics were 10.9 percent of women affecting 446,137 infants in the first trimester of pregnancy, 1.4 percent of women affecting 57,302 infants in the second, and 0.7 percent of women affecting 28,651 infants in the third trimester (Young, 2006, p. 11). Roughly 4 million live births are recorded annually in the United States (Young, 2006, p. 16).

The 2006 NSDUH Report, which combined data collected during 2005 and 2006, indicated that among pregnant women between 15 and 44 years old, only four percent reported use of illicit drugs during the previous 30-day period; the rate among the non-pregnant, age-matched cohort was 10 percent (p. 25). In the same age group, 11.8 percent of pregnant women reported current use of alcohol, 2.9 percent reported binge drinking, and 0.7 percent indicated that they drank heavily. Among the non-pregnant group, the results for those categories were 53.0 percent, 23.6 percent, and 5.4 percent. Binge drinking of alcohol decreased from 10.9 percent to 4.6 percent during the first trimester, as reported in 2002–2003 (p. 34). The rates of tobacco use/cigarette smoking were also lower among pregnant than non-pregnant women between the ages of 18 and 25: 25.6 percent and 35.6 percent, respectively. Among those between the ages of 26 and 44, the rates of tobacco use were 10.3 percent for pregnant women and 29.1 percent for those who were not pregnant. In contrast, the rate for girls between the ages of 15 to 17 was higher in the pregnant than in the non-pregnant group: 23.1 percent and 17.1 percent, respectively (p. 44).

A pregnant drug-dependent woman puts her developing fetus at risk for a number of diseases, including hepatitis, human immunodeficiency virus (HIV), tuberculosis, and sexually transmitted diseases (STDs). A number of these diseases may be acquired through needle sharing. Mothers who are infected with these diseases are likely to deliver prematurely.

HEROIN AND METHADONE

In pregnant women who use heroin, the placenta typically shows microscopic evidence of oxygen deprivation. Infants are small for their gestational age, and all their organ systems are affected. In heroin-dependent women, a significant portion of the medical complications seen in their newborns is due to prematurity and low birth weight. Such complications include immature lungs, difficulties in breathing at birth, brain hemorrhage, low sugar and calcium levels, infections, and jaundice.

Women on methadone maintenance (an oral narcotic used for the treatment of heroin addiction) are more likely to give birth to normal- or almost normal-sized babies. Because they are in treatment, the complications in their infants are not as severe and generally reflect: (a) the amount of prenatal care the mother has received; (b) whether the mother has suffered any complications, including hypertension or infection; and, most importantly, (c) any multiple drug use that may have produced an unstable intrauterine environment for the fetus, perhaps complicated by withdrawal and/or overdose.

Multiple drug use may cause a series of withdrawals when the pregnant woman cannot obtain the drug she needs. This series of extreme physical conditions in the pregnant woman can severely affect the oxygen and nutrients that feed the developing fetus, causing various birth defects depending on when in each trimester the withdrawals occur. If the mother overdoses, a decreased oxygen supply to the fetus can cause aspiration pneumonia—if the mother survives the overdose to give birth.

Laboratory and animal studies have shown that opioids may have an inhibitory effect on enzymes that influence oxygen metabolism. They also alter the passage of oxygen and nutrients to the fetus by constricting the umbilical vessels and decreasing the amount of oxygen delivered to the developing fetal brain. Such metabolic side effects may cause a derangement in the acid/base balance (acidosis). In contrast, increased maturation of organ systems and certain enzymes have been seen in heroin-exposed infants, including maturation of the lungs, tissue-oxygen unloading, sweat glands, and liver enzymes. The stressful life of the pregnant woman probably contributes to this enhanced maturation in heroin-exposed infants.

The genetic risks to the offspring of addicts on heroin *and* methadone include an increase in the frequency of chromosome abnormalities; infants

exposed predominantly to methadone *in utero* do not experience the same vulnerability to those abnormalities. The adverse environmental factors that may contribute to the abnormal findings in heroin-exposed infants may be less prominent in methadone mothers, as drug addiction is almost always compounded by poor maternal nutrition, extreme stress, infectious disease, and a lack of early and consistent prenatal care. However, in the absence of specific clinical abnormalities, it is impossible to isolate either methadone or heroin as agents linked to genetic damage. Given the obstetrical and medical complications, the lack of prenatal care, and the prematurity of the infants at delivery, it is not surprising that the death rate for addicted babies is higher than for infants born to non-addicts.

NEONATAL ABSTINENCE SYNDROME

The term neonatal abstinence syndrome (NAS) refers to the continuum of signs and symptoms evidenced by infants born to substance dependent mothers. Prenatally, NAS primarily describes the physiological, psychological, and cognitive impacts of substance use/abuse on the developing fetus. These impacts may be apparent at, or shortly after, birth or may not be detected until the child is older and develops learning, medical, or behavioral difficulties.

Whether born to heroin-addicted or methadone-dependent women, most infants seem physically and behaviorally normal at birth. The onset of their withdrawal may begin shortly after birth to two weeks of age, but most develop symptoms within seventy-two hours of birth. If the mother has been on heroin alone, 80 percent of the infants will develop clinical signs of withdrawal between four and twenty-four hours of age. If the mother has been on methadone alone, the baby's symptoms usually appear within forty-eight to seventy-two hours. The time of onset of withdrawal in individual infants depends on the type and amount of drug used by the mother, the timing of her last dose before delivery, the character of her labor, the type and amount of anesthesia and pain medication given during labor, and the maturity, nutrition, and presence or absence of systemic diseases in the infant.

Postnatal NAS includes the constellation of sequelae (secondary consequences) of maternal substance use, both developmental and medical. When first studied, the presence of NAS applied to the after-birth syndrome seen in infants born to heroin- or methadone-using mothers; over time it was broadened to include the aftereffects of cessation of virtually any chronic substance use—whether prescription medications used to control physiological or behavioral health disorders (such as seizures, depression, mood disorders, or other chronic medical or mental health conditions), as well as alcohol, tobacco, or illicit drugs used either recreationally or as a result of dependence. NAS is the most pronounced in infants born of women using opioids or narcotics.

Multiple, or polydrug, use increases the likelihood and severity of NAS. Infants born to mothers using stimulants, such as cocaine, methamphetamine, MDMA (Ecstasy), or medications used to treat ADHD (attention deficit hyperactivity disorder), often do not experience classic NAS, but show symptoms more closely associated with ongoing effects of the exposure to those substances. Drugs with a shorter half-life produce withdrawal effects more quickly after they are discontinued.

NAS typically involves multiple systems, with the greatest number of symptoms involving the central nervous and gastrointestinal systems. The type, number, and severity of symptoms will depend, to a large extent, on duration, amount, and frequency of drugs used as well as on the infant's own metabolism and physiological maturity. Opiates produce the most severe and obvious NAS effects and include premature birth, low birth weight for gestational age, and intrauterine growth retardation (IUGR). The effects of methadone use on the fetus are similar to those of heroin. It has a longer half-life, so acute NAS symptoms occur later, possibly even up to four weeks after birth.

Babies with NAS often exhibit signs and symptoms of central nervous system hyperirritability, gastrointestinal dysfunction, respiratory distress, and autonomic nervous system symptoms that include excessive yawning and sneezing, sweating, mottling, and fever. These infants frequently develop tremors that progress in severity. High-pitched crying, increased muscle tone, irritability, and exaggerated infant reflexes are common. Sucking of fists or thumbs is common, yet when fed, the infants have extreme difficulty in eating, and vomit

frequently because of an uncoordinated and ineffectual sucking reflex. The infants may develop diarrhea and are therefore susceptible to dehydration and electrolyte imbalance. At birth the level of drug(s) in the blood begins to fall, and the newborn continues to metabolize and excrete the drug(s); withdrawal signs occur when critically low levels have been reached.

Studies indicate that more full-term infants require treatment for withdrawal than do preterm infants. Because withdrawal severity appears to correlate with gestational age, less mature infants show fewer symptoms. Decreased symptoms in preterm infants may be due to either (a) developmental immaturity of the preterm nervous systems, or (b) reduced total drug exposure because of shorter gestations.

The most severe withdrawal occurs in infants whose mothers have taken large amounts of drugs over a long period of time. Usually, the closer to delivery a mother takes heroin, the greater the delay in the onset of withdrawal and the more severe the baby's symptoms. The duration of symptoms may be anywhere from six days to eight weeks. The maturity of the infant's own metabolic and excretory mechanisms plays an important role. Although the infants are discharged from the hospital after drug therapy is stopped, some symptoms such as irritability, poor feeding, inability to sleep regularly, and sweating may persist for several months.

Drug-exposed infants show an uncoordinated and ineffectual sucking reflex as a major manifestation of withdrawal. Regurgitation, projectile vomiting, and loose stools may complicate the illness further. Dehydration, due to poor intake coupled with excessive losses from the gastrointestinal tract, may cause malnutrition, weight loss, subsequent electrolyte imbalance, shock, coma, and death. Untreated neonatal withdrawal carries a risk of death. The infant's respiratory system is also affected during withdrawal: Excessive secretions, nasal stuffiness, and rapid respirations are sometimes accompanied by difficulty breathing, blue fingertips and lips, and cessation of breathing. Severe respiratory distress occurs most often when the infant regurgitates, aspirates, and develops aspiration pneumonia.

PRENATAL OPIOID EXPOSURE

In addition to the heroin and methadone effects listed above, newborns exposed to opiates *in utero* are at increased risk for fetal distress or death or sudden infant death syndrome (SIDS). Thrombocytosis, an excessive production of platelets in the blood that can lead to blood clots, often occurs within the first few weeks of life and may last for several months.

PRENATAL STIMULANT EXPOSURE

Stimulants such as cocaine, amphetamines, and methamphetamine cross not only the blood–brain barrier of the mother, but the placental barrier as well. Stimulants have potent effects on the brain and cause prevention of reuptake or physiological alteration of several important neurotransmitters (substances that transmit nerve impulses), such as dopamine, epinephrine, norepinephrine, and serotonin. Infants exposed to stimulants often have an exaggerated startle reflex, a larger than normal Moro reflex (when exposed to a sudden noise, babies flex their legs and extend their arms abruptly), an excessive need to suck, and general jitteriness and irritability. There is ongoing research on the relationship between prenatal stimulant exposure and head circumference as well as on the long-term impact on the development of the brain.

Exposure is causally linked to smaller head circumference and therefore delayed brain development. Although most children do catch up in terms of overall head/brain growth over the first few years of life, there is a significantly increased rate of learning disabilities among children prenatally exposed to drugs, particularly in the areas of reading and math, as well as attention deficit disorders.

PRENATAL CAFFEINE AND TOBACCO EXPOSURE

Mothers who have excessive intake of caffeine (in any form) transmit a substance called methylxanthine to fetuses and breastfed infants. Tobacco use intensifies the effects of the drug on the fetus, because the blood vessels of the placenta increase their concentration in the developing infants' blood systems by up to 15 percent above that experienced by the mother. Tobacco use during pregnancy increases the likelihood of low birth weight and tobacco withdrawal in the neonate.

Exposure to either substance impairs the newborn's ability to habituate, to orient by sight or sound, to develop appropriate physiological

mechanisms for autonomic regulation, and to be comforted. It can also cause a hyperreactive startle reflex, tachycardia, irritability, inefficient circulation, poor feeding, and tremors in the neonate—all indicators of nicotine toxicity in the body.

Behavioral studies have also been conducted with children exposed to prenatal smoking. Some research has shown that a child whose mother smoked during pregnancy is at increased risk of becoming a smoker. Because smoking activates neurotransmitters in the brain—including dopamine, which is involved in reinforcing the effects of addictive drugs—researchers have speculated that nicotine may have an effect on the developing dopamine system of the fetus and put the child at greater risk of addictive behavior in later life.

Prenatal exposure to cigarette smoking may affect a growing fetus in several ways. Carbon monoxide and high doses of nicotine obtained during inhalation of tobacco smoke can interfere with the oxygen supply to the fetus. Nicotine readily crosses the placenta, and it likely causes vasoconstriction of the umbilical arteries and impedes placental blood flow. Carbon monoxide can bind with hemoglobin to reduce the capacity of the blood to transport oxygen. These factors combined likely account for the developmental delays commonly seen in fetuses and infants of smoking mothers.

One of the most striking risks associated with prenatal smoking is that of Sudden Infant Death Syndrome (SIDS). A higher mortality rate exists for infants whose mothers have smoked compared to those who have not. Maternal smoking during pregnancy has also been cited as a major risk factor in almost every epidemiologic study of SIDS. The risk of sudden infant death syndrome is greater among infants exposed to both prenatal and postnatal smoking compared to those only exposed to postnatal smoking. The increase in SIDS risk also appears to be related to the *dose* of passive smoke to which the fetus or infant is exposed: The greater the exposure to smoke both before and after birth, the higher the risk of SIDS.

PRENATAL MARIJUANA EXPOSURE

To date, no research has shown the presence of a withdrawal syndrome in infants whose mothers used marijuana. However, prenatal exposure to marijuana may cause brain bleeds, jitteriness, sepsis (severe infection), excessively low calcium, hypoglycemia, hypoxic encephalopathy (lack of sufficient oxygen to the developing brain causing brain damage, possibly resulting in mental retardation, developmental delays, or other neurophysiological deficits), and IUGR—particularly involving weight, length, and head circumference. The greater the mother's drug use during pregnancy, the more pronounced and severe the symptoms in the neonate. Nicotine toxicity effects, as mentioned above, may also be present. Although cognitive effects may last for several years, catch-up physiological growth typically occurs during the first year.

ANTIDEPRESSANT AND MOOD STABILIZER EXPOSURE

Pregnant women who use antidepressants (such as selective serotonin reuptake inhibitors, or SSRIs) or other mood stabilizers during their last trimester sometimes give birth to infants who express NAS. The signs and symptoms of NAS may include irritability, tremors, agitation, rapid and shallow breathing, stuffiness and nasal discharge, vomiting, and diarrhea. These effects are short in duration and generally only last for the first week or two of life.

T'S AND BLUES AND OXYCODONE EXPOSURE

T's and Blues are the street name for an intravenously injected drug cocktail comprised of a prescription painkiller called pentacozine (an opioid similar to morphine) and a nonprescription allergy medication. Babies born to women using this drug typically have reduced birth weight, may grow more slowly than their same-aged peers, and may experience withdrawal symptoms similar to infants with prenatal opioid exposure. The same is true for infants prenatally exposed to oxycodone.

PRENATAL CLUB DRUG EXPOSURE

Club drugs such as PCP (angel dust), ketamine (Special K), and lysergic acid (LSD), when used by pregnant women, may lead to NAS in the newborn. Prenatal exposure to these club drugs may result in learning and behavioral problems that endure.

PRENATAL MDMA (ECSTASY) EXPOSURE

There have been a small number of longitudinal human studies of the prenatal effects of MDMA to

date. Thus far, the research suggests that use of MDMA during pregnancy may lead to permanent neurobiological changes; behavioral abnormalities such as hyperactivity; attention, focusing, and concentration deficits; and learning impairments.

PRENATAL INHALANT OR SOLVENT EXPOSURE

Women using inhalants (such as spray paint or gasoline fumes) or solvents (such as glues and resins) are at risk of kidney, liver, and brain damage; the mortality rate among this group of users is particularly high. Pregnant women who use them are at higher risk for miscarriage. Pregnancies that remain viable have increased incidence of premature birth, low birth weight, IUGR, and birth defects.

NAS ASSESSMENT AND MANAGEMENT

With proper management, the neonate's prognosis for recovery from the acute phase of withdrawal is good. When symptoms of withdrawal appear, simple nonspecific measures should be instituted, such as gentle, infrequent handling, maintaining calm and quiet surroundings, avoiding bright lights, swaddling, and feeding on demand. Careful attention to fluid-electrolyte balance and calorie support is essential, particularly in opioid-exposed infants undergoing withdrawal, because they display uncoordinated sucking and poor feeding, often develop vomiting and diarrhea, and have increased water loss due to rapid respirations and sweating.

Indications for specific treatment, dosage schedules, and duration of treatment have varied widely. As a general guide, if, in spite of nonspecific measures, babies have feeding difficulties, diarrhea, marked tremors, irritability even when undisturbed, or cry continuously; they should be given medication to relieve discomfort and prevent dehydration and other complications. Dosages must be carefully regulated to minimize symptoms without excessive sedation. Extremely low doses of drugs such as antiepileptic medications and mild opiates are effective in treating narcotic withdrawal symptoms in the infant.

NEUROBEHAVIOR IN NEWBORNS

Researchers using well-studied and clinically accepted neonatal assessment scales in evaluating drug-exposed infants noted that they were less able than non-drug-exposed infants to stay alert and less able to orient to auditory and visual stimuli; these effects were most pronounced at 48 hours of age. Drug-exposed infants were generally as capable of self-quieting and responding to soothing intervention as normal neonates, although they were substantially more irritable. These findings have important implications for caregivers' perceptions of infants, and thus may have long-term impact on the development of infant-caregiver interaction patterns.

On measures of social engagement, interactions between drug-dependent mothers and their infants have shown abnormalities. Abnormal interaction was explained by less positive maternal attachment as well as difficult infant behavior, which impedes social involvement. Many of these interactive abnormalities reverted to normal by four months of age, but the need for parenting training is obvious.

SUDDEN INFANT DEATH SYNDROME

Sudden infant death syndrome (SIDS) is defined as the sudden and unexpected death of an infant between one week and one year of age; the child's death remains unexplained after a complete autopsy examination, a full history, and a death-site investigation. Compared to an incidence of approximately 0.55 per 1,000 live births in the general population, narcotic-exposed infants appear to have an increased risk of SIDS. Other high-risk factors for SIDS, such as low socioeconomic status, low birth weight, young maternal age, membership in a racial minority group, and maternal smoking, were all overrepresented in studies of drug-using groups. In a large-scale study, New York City SIDS rates were calculated in 1.2 million births from 1979 to 1989. Maternal opiate use, after controlling for high-risk variables, increased the risk of SIDS by three to four times that of the general population.

LONG-TERM OUTCOMES FOR CHILDREN

Although a drug-exposed newborn may seem free of physical, behavioral, or neurological deficits at the time of birth, the effects of pharmacological agents (used or abused) may not become apparent for many months or years. Although heroin abuse during pregnancy has been recognized for more than fifty years and methadone treatment has been

employed for more than thirty years, longitudinal follow-up of opioid-exposed infants is still fragmentary. The difficulties encountered in long-term follow-up of this population include an inability to fully document the mother's drug intake, difficulty separating the drug effects from high-risk obstetric variables, problems in maintaining a cohesive group of infants for study, and the need to separate drug effects from those of parenting and the home environment.

The easiest part of caring for the neonate is actually over when drug therapy has been discontinued and the infant is physically well. The most difficult parts then begin—the care involved in discharge planning and assuring optimal growth and development throughout infancy and childhood. Because there is no standard for the disposition of these infants, some may be released to their mothers, some to relatives, and others placed in the custody of a state agency. Other infants may be voluntarily released by their mothers to private agencies for temporary or permanent placement.

In the United States pressure to separate infants from their addicted mothers has been growing. This solution may not be practical in cities where social services and courts are already understaffed and overworked. There is a nationwide shortage of appropriately trained, licensed, and available foster parents qualified to care for high-risk infants. Pediatricians typically believe that the mother-infant association should not be dissolved except in extreme situations. In addition to intensive drug rehabilitation and medical treatment, these women need extensive educational and job training to become productive citizens and loving mothers who will positively socialize their children. Supportive therapies, such as outpatient care or residential treatment, may help eliminate some of the medical and social problems experienced by drug-dependent women and their children.

Most of the children evaluated for long-term development have been exposed to methadone. Evaluations have occurred at various intervals: at 6, 12, 18, and 24 months; then at 3, 4, and 5 years of age. Testing procedures utilized include the Gesell Developmental Schedule, the Bayley Scales of Infant Development, the McCarthy Scales of Infant Abilities, the Stanford-Binet, and the Wechsler Preschool and Primary Scale of Intelligence. Infants exposed to drugs prenatally have shown overall developmental scores in the normal range but a tendency to decrease in scores at about two years of age, which suggests that environment may confound long-term infant outcome. Low socioeconomic groups suffer from this factor particularly because of poor language stimulation and development.

The developmental scores in these early years, although useful in identifying areas of strength and weakness, are not valid predictors of subsequent intellectual achievement. Many studies have proposed multiple-factor models to assess infant outcome following intrauterine drug exposure. One such postnatal influence involves maternal-infant interaction. Drug-exposed infants are often irritable, have decreased rhythmic movements, and may display increased muscle tensing when handled. Mothers may interpret such behaviors as rejection, leading to inappropriate maternal caretaking and possible neglect of the infant. Studies of mother-infant interactions indicate that (a) infants born to narcotic-addicted women show deficient social responsiveness after birth; (b) this deficient mother-infant interaction persists until the infants' treatment for withdrawal is completed; and (c) maternal drug dosages may affect that interaction.

Available data suggest that at five years of age, children born to women maintained on methadone, in contrast to heroin-exposed babies, generally appear to function within the normal developmental range. In addition, no significant differences in language and perceptual skills were observed between them and a matched control group consisting of children of mothers not involved with drugs. Difficulty in following large cohorts (study groups) of drug-exposed infants has led to the study of very limited samples.

Positive and reinforcing environmental influences can significantly improve drug-exposed infant development. Women who show a caring concern for their infants are most likely to pursue follow-up pediatric care and cooperate in neurobehavioral follow-up studies. Lacking a large database, there is a significant need for comprehensive studies assessing the development of large populations of drug-exposed infants.

See also **Alcohol- and Drug-Exposed Infants; Attention Deficit Hyperactivity Disorder; Complications: Route of Administration; Fetal Alcohol Syndrome; Pregnancy and Drug Dependence.**

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FINLAND. *See* **Nordic Countries (Denmark, Finland, Iceland, Norway, and Sweden).**

FLY AGARIC. A poisonous mushroom of Eurasia (*Amanita muscaria*), having typically a bright red cap with white dots. A preparation, consisting primarily of the dried mushroom, is ingested by the people of Siberia as a hallucinogen. Intoxication by ingestion of several mushrooms

moistened with milk or fruit juice leads to a progression of symptoms—beginning with tremors, continuing through a period of visual hallucination that may be interpreted as having religious significance, and finally ending in deep sleep. A similar preparation may be identified with the deified intoxicant *soma* of the ancient Hindus. In some cultures, the urine of intoxicated individuals is ingested by others to induce intoxication, since the active components of the preparation pass unmetabolized through the body.

The active components found in fly agaric are ibotenic acid and several of its metabolites. The predominant metabolite is muscimol, which has agonist properties at a subset of receptors recognizing the neurotransmitter GABA. Ibotenic acid itself has agonist properties at certain excitatory amino acid receptors and has been shown to be neurotoxic.

See also **Plants, Drugs From.**

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FOREIGN POLICY AND DRUGS, UNITED STATES. Drug control is a relative newcomer to the list of global issues that are now an integral part of U.S. foreign policy. Although arms control and human rights were already important international issues in the 1970s, drug control lagged behind. In 1971 and 1972 some members of Congress tried to impose foreign-aid restrictions on Turkey to stop the entry of its heroin, but the U.S. government did not want to risk hurting relations with an important defense ally over heroin, which was not then considered a mainstream drug. The government instead found a compromise through diplomatic efforts, which led to the Turkish government severely limiting the cultivation of opium poppies (from which heroin is made) and changing the way in which poppies were processed into legitimate medicinal opium. Parallel diplomatic negotiations with Mexico resulted in cooperation on marijuana eradication efforts. On the international front, the U.S. government pressed hard for the ratification of the 1971 United Nations (UN) Convention on Psychotropic Drugs and created the UN Fund for Drug Abuse Control (UNFDAC), the predecessor of today's UN Drug Control Program (UNDCP). During the rest of the decade, however, drug control gradually declined as a key U.S. foreign policy objective.

Drug control only gained full diplomatic legitimacy in the 1980s when cocaine use became widespread among entertainers, athletes, and stockbrokers. U.S. relations with the government of Panama and its leader, General Manuel Noriega, soured when it became clear that Noriega had cooperated with the Medellin drug cartel. A U.S. federal grand jury in Miami indicted Noriega on drug-trafficking charges in 1988, alleging that he had facilitated money laundering by the cartel and permitted the cartel to operate cocaine-processing facilities in Panama. In 1989 the United States invaded Panama and brought Noriega to Florida for a trial. In 1992 he was convicted on the drug-trafficking charges and sentenced to 40 years in prison.

Despite targeted efforts on prominent officials such as Noriega, the government's inability to stop the drug epidemic at home prompted Congress to address the role of foreign governments in drug trafficking. In 1986, in the first of a series of comprehensive international antidrug laws (the Anti-Drug Abuse Act of 1986), Congress placed the burden of halting drug flows on the governments of the drug-producing countries. Using a traditional carrot-and-stick approach, the law required the major drug-producing and transit countries to cooperate fully with the United States in drug matters in order to receive American foreign aid. Half of all assistance was withheld every year until the office of the president certified that the country concerned had met the criteria for receiving aid. Subsequent laws have expanded this requirement, obliging the major drug-producing and transit countries to also comply with the 1988 UN Convention against Illicit Traffic in Narcotics Drugs and Psychotropic Substances. Countries that do

not comply not only lose U.S. assistance but also incur U.S. opposition to loans from the World Bank and other international financial institutions. For many countries in the developing world, losing access to these loans is an even greater hardship than losing U.S. assistance. Although the certification process has raised tensions with some foreign governments, it has become an accepted part of U.S. foreign policy. However, critics note that the United States has recertified countries such as Mexico and Colombia, despite the political corruption in these nations that has seriously undercut narcotics enforcement efforts.

In earning its diplomatic legitimacy, drug control has had to overcome the same obstacles encountered by other global issues, such as human rights or nuclear nonproliferation. The U.S. foreign policy establishment has favored strategic issues affecting vital U.S. national security or trade interests over law enforcement or scientific endeavor. It has been reluctant to allow multilateral "functional" questions to affect traditional bilateral negotiations. However, after the terrorist attacks on September 11, 2001, the State Department placed greater emphasis on drug control. It maintains that counternarcotics programs complement the war on terrorism, both directly and indirectly, by promoting the modernization of and supporting operations by foreign criminal justice systems and law enforcement agencies charged with the counterterrorism mission.

Congress has consistently worked to keep drug control high on the list of U.S. foreign policy issues. By denying virtually all forms of aid—excluding humanitarian and drug-control assistance—to countries that refuse to cooperate, Congress has devised an effective form of leverage over drug countries. Because the law also allows the president to waive sanctions when clearly stated national interests are at stake, Congress has made it difficult for foreign policy agencies to evade their drug-control responsibilities.

RESPONSIBLE AGENCIES

The U.S. Department of State is responsible for formulating international drug policy. Its Bureau for International Narcotics and Law Enforcement Affairs oversees the annual certification process and prepares an annual report. Since 1989 formal coordination authority has rested with the White House Office of National Drug Control Policy (ONDCP) and the National Security Council. Drug-control programs, however, involve a broad spectrum of government agencies, including the Central Intelligence Agency, the Department of Defense, the Department of Homeland Security (which now includes the U.S. Customs Service and the Coast Guard), the Department of Treasury, the Justice Department, the Drug Enforcement Administration, and the Department of Health and Human Services. A small percentage of the U.S. drug-control budget is spent on international programs. The bulk of the money goes to domestic law enforcement, drug treatment, and public education.

THE REALITIES OF DRUG CONTROL

As presidential administrations have discovered, an effective drug policy is easier to design than to carry out. The drug issue is a typical chicken-and-egg problem. Does supply drive demand or vice versa? Drug-consuming countries traditionally blame the suppliers for drug epidemics, whereas drug-producing countries allege that without foreign demand, local farmers would not grow the drug crop at all. Planners must therefore strike the right balance between reducing drug supply and demand. In theory, eliminating drug cultivation in the source countries is the most economical solution, because it keeps drugs from entering the system and acquiring any value as a finished product. Few source-country governments—all of which are in developing nations—will, however, deprive farmers of a livelihood without substantial compensation from abroad. And the price they seek is usually more than the U.S. government is prepared to pay.

THE NATURE OF THE THREAT

The illegal drug trade in the early twenty-first century is one of the most lucrative, and therefore powerful, criminal enterprises in history. Drugs generate profits on a scale without historical precedent—especially given their abundance and low production costs. Such financial resources, which are well beyond those of most national budgets, give drug traffickers the means to buy sophisticated arms, aircraft, and electronic and technical equipment available to few countries. More importantly,

illegal drug revenues allow trafficking organizations to buy themselves protection at almost every level of government in the drug-producing and drug-transit countries, where drug-related corruption remains the single largest obstacle to effective control programs.

Efforts to control the quantity of drugs have had mixed results. Opium production, which declined in the years 2001 to 2006, rebounded in 2007. Opium poppy cultivation in Southeast Asia increased by 22 percent in 2007, mainly driven by a 29 percent increase in opium cultivation in Myanmar (the former Burma) and increased cultivation in Afghanistan. In South America, coca production has been reduced, yet it is enough to satisfy world demand twice over. This surplus is so large that the drug trade easily absorbs losses inflicted by drug-control authorities and still makes enormous profits.

Traffickers have the option of expanding the cultivation of drug crops into new areas. For example, although coca plants are currently confined to Latin America, coca once flourished in Indonesia and could do so again if market conditions were right. Opium poppy cultivation is spreading into nontraditional areas, including South America. South American cocaine-trafficking organizations have diversified into opium poppy cultivation. Without active government antidrug programs, production will grow until the new expanding market is saturated.

The popularity of methamphetamine grew dramatically in the United States beginning in the late 1990s. Local meth labs were the original source of most meth consumed in the United States, but state and federal laws have severely restricted the availability of the chemicals needed to produce it. Consequently the illegal production of meth in Mexico and its importation to the United States have become a major problem. By 2008 the majority of meth consumed in America came from Mexico.

EARLY-TWENTY-FIRST-CENTURY POLICY

The U.S. government's first priority is to stop the flow of cocaine, which still poses an immediate threat to potential drug users. Because of rising heroin use promoted by the new, cheaper Latin American producers, the United States must also focus on opium-producing countries. The U.S. goal is to limit the cultivation of drug crops to the amount necessary for international medical applications. Because all the cocaine that enters the United States comes from coca plantations in Peru, Bolivia, and Colombia, the U.S. government maintains active drug-control programs in these three countries. During the 1990s the United States also assisted Bolivia and Peru in their efforts to reduce coca cultivation. Although these efforts dramatically reduced production, drug traffickers increased coca production in Colombia. This resulted in increased political corruption and political destabilization. In 2000 the United States approved $1.3 billion in emergency assistance for Colombia; the aid package contained money for police and military training, administration of justice programs, and economic development programs. The United States has also increased its military assistance to Latin America to help fight narcotics trafficking. Although Colombia leads the world in coca cultivation and is the source of 90 percent of the cocaine entering the United States, by 2008 it had made some progress in combating cultivation. In 2007, with U.S. assistance, Colombia eliminated a record-breaking 153,000 hectares of coca through aerial eradication and another 66,000 through manual eradication.

Opium control is more difficult than coca suppression, because most of the world's opium poppy grows in countries where the United States has minimal diplomatic influence (Myanmar, Laos, and Iran). The U.S. military presence in Afghanistan since 2001 has not led to the destruction of the opium trade. In 2007 that nation produced 90 percent of the world's opium poppy. As the former leaders of the Taliban government have regained control of the southern provinces, they have used increased opium production to fund the insurgency.

AN INTERNATIONAL APPROACH

Because bilateral programs seldom provide solutions to global problems, the United States has been an active proponent of collective action under the 1988 UN Convention. This latest agreement covers not only the traditional aspects of drug production and trafficking but also requires signatories to control drug-processing chemicals and outlaw drug-money laundering. The money-laundering provisions are critical innovations, as they target the enormous international cash flows that sustain

the drug trade. As astronomical as drug profits may be, drug money is useless unless it can enter the international banking system. The major industrialized countries are therefore pressing for uniform laws and regulations to exclude drug money in all key financial centers. If honestly implemented, strict money-laundering controls, along with better use of existing programs to suppress drug supply and decrease consumption, offer the hope of reducing the drug trade from an international threat to a manageable concern. However, efforts by the European Union (EU) to create a uniform set of procedures to combat this problem have been flawed. A 2006 review by an EU committee found that procedures for identifying and reporting suspicious transactions differed between countries. Some members took too long to report suspicious deals, ruling out action.

See also **Bolivia; Coca/Cocaine, International; Colombia; Crop Control Policies; Drug Interdiction; Drug Laws: Financial Analysis in Enforcement; Golden Triangle as Drug Source; International Drug Supply Systems; Opium: U.S. Overview; Peru; Terrorism and Drugs; U.S. Government Agencies.**

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FRANCE. France is a western European country with a population of about 60 million. It belongs to the European Union and uses the Euro; however, many of the available statistics through the 1990s are in francs. It is the leading world consumer and exporter of alcoholic beverages. Drinking wine with meals has deep cultural roots in France. Tobacco was long a monopoly of the state, and its use is still widespread. There has long been a small traffic of illicit drugs. In the last third of the twentieth century, an increase was observed in the use of illicit drugs, chiefly cannabis, among youths. The French government has developed several programs, mainly since the 1990s, to protect the public's health from the harm caused by these substances.

GEOGRAPHY

France is at the Western end of Europe. It produces its own alcoholic beverages and tobacco products, along with some imports. Its cannabis comes mainly from Morocco, usually by way of Spain. Cocaine and crack come from the new world, often by way of the French Antilles. Opium is produced chiefly in Afghanistan; heroin is produced in Turkey and other countries and travels through Germany and various European countries to reach France.

HISTORY

Alcoholic Beverages. Wine has been used in the diet since antiquity, and spirits were used medically since the late middle ages. In the nineteenth century the consumption of wine nearly quadrupled (from 33 to 120 liters per capita between 1830 and 1900), and use of beer and spirits markedly increased in all classes of society. Inebriety became more prominent. Temperance movements emerged after 1870 (Societé Française de Tempérance, 1872; Union Française Antialcoolique, 1894; Ligue Nationale Antialcoolique and Fédération Ouvrière Antialcoolique, both early in the 1900s). Members of the movement took a moral stance. Calls for governmental control over alcohol increased during World War I, and absinthe drinks were made illegal in 1915. After World War I the temperance movement collapsed (Brennan, 1989). Use of alcoholic beverages gradually increased

until concern about alcohol-related health problems emerged in the 1950s. During his brief tenure as prime minister, Pierre Mendès-France initiated several proposals and decrees to reduce alcohol production and consumption, but he encountered great resistance from the wine industry as well as the public (Ugland, 2003). However, attention to alcohol-related harm had increased. A governmental High Committee for Study and Information about Alcoholism was formed in 1954. Government intervention to decrease alcohol use, especially among youths, intensified in the 1990s.

Tobacco. Tobacco was introduced in France early in the sixteenth century. Jean Nicot popularized it for medical purposes in the 1560s. In the next century it became fashionable to use it as snuff or for pipe smoking. The first commercial cigarettes were produced in 1843 by the Manufacture Française des Tabacs, a state run outfit that started the French government monopoly on tobacco. The French monopoly was later know as SEIT (Service d'Exploitation Industrielle des Tabacs), and its profits were used from 1926 on to reduce the public debt. In 1935 it became SEITA by adding a monopoly on matches (*allumettes*). In 1959 it became a public establishment to manage the state monopoly. In 1984 the State became the only investor in SEITA. In 1995 SEITA was privatized, and in 1999 it fused with Tabacalera, a Spanish tobacco monopoly to become Altadis. Altadis is now the sixth-largest producer of cigarettes in the world and the first of cigars (Tabagisme.net).

World War I markedly increased the use of tobacco by soldiers who kept the habit after discharge. Prevalence of smoking steadily increased during the first three-quarters of the twentieth century. Knowledge of the causal role of tobacco in lung cancer, in other cancers, and in heart disease spread in the 1970s. Laws to control tobacco advertising and smoking in public places were passed in 1976 and 1991.

Illicit Psychoactive Substances. Cannabis, opium derivatives, and cocaine have been used in France for several centuries for both medicinal and recreational use. LSD, hallucinogenic mushrooms, ecstasy, and amphetamines were introduced after the middle of the twentieth century. The twentieth century saw an increase in nonmedical use of psychoactive pharmaceuticals. Initially, these drugs were used by a relatively small number of people looking for new sensations and by socially marginalized people. In the 1960s youths began to experiment with, and eventually use, many of these drugs. In subsequent years cannabis became very widely used by teenagers and young adults. Use of pharmaceutical drugs has increased steadily, especially among girls. The government responded with a punitive law in 1970, followed in the 1990s by risk reduction measures. In the past two decades a large set of governmental structures has been organized to integrate the various actors in the fight against drugs.

THE FIGHT AGAINST DRUGS

No single agency or ministry is charged with coordinating the various aspects of the fight against drugs in France at the national level; rather, control is divided among several ministries. State control of drug use includes the Ministry of Justice and the law courts. The Ministry of the Interior is in charge of the police in localities with more than 100,000 residents, whereas the Ministry of Defense oversees the *gendarmerie* (police) in rural areas and small towns. Assistance to drug users has been primarily a function of the Ministry of Health; however, social services have become increasingly involved. Several other agencies are also involved, such as customs in the Ministry of Treasury or the newly-created Ministry of Research. In order to create some coherence among these various activities, the French government has established two bodies: Mission Interministerielle de Lutte contre la Drogue et la Toxicomanie (MILDT), and the Observatoire Français des Drogues et des Toxomanies (OFDT).

The MILDT was founded in 1982 as a task force and elevated in 1996 to its present title and rank, reporting directly to the prime minister. It prepares government plans for the fight against drugs and monitors the implementation of these plans. It coordinates the policies of 17 ministries and supports the work of several other state and private partners, including local governments, specialized institutions, professional bodies, and associations. It also finances public interest groups. Its budget comes from the various ministries. (MILDT, 2004)

The OFDT is one of the public interest groups financed by MILDT. It is charged with the collection, analysis, synthesis, and distribution of data

concerning alcohol, tobacco, cannabis, and other psychoactive drugs in France. Their statistics are secondary analyses based on primary data from various public or private surveys. Statistics are available at OFDT for number of sales, level of consumption, associated morbidity and mortality, and methods of repression of prohibited use and of traffic. (OFDT, 2006)

CURRENT SUBSTANCE USE

National surveys (ESCAPAD in 2003 and 2005 and Barometer Santé 2005) provided the following quantitative information on the adult population aged 12 to 75. Adults who had used psychoactive substances at least once in their lifetime numbered 42.5 million for alcohol, 34.8 million for tobacco, 15.1 million for psychotropic medications, 12.4 million for cannabis, 1.1 million for cocaine, 0.9 million for ecstasy, and 0.36 million for heroin. Adults who used the substance daily numbered, in millions, 6.4 for alcohol, 11.8 for tobacco, and 0.55 for cannabis (OFDT, 2006).

In 2005 a study of 17-year-olds showed the following percentage of monthly usage in the study population: 82 percent of boys and 75 percent of girls for alcohol, 41.5 and 40.9 for tobacco, 33.5 and 22.5 for cannabis, 3.7 and 11.8 for psychotropic medications, 1.7 and 1.0 for ecstasy, 1.2 and 0.7 for cocaine, 1.0 and 0.5 for amphetamines, 0.54 and 0.3 for LSD, 0.3 and 0.2 for heroin, and 0.32 and 0.1 for crack (OFDT, 2006).

Alcohol. There has been a steady decrease in alcohol sales since the 1950s. Sales expressed in liters of pure alcohol per resident decreased from 15.7 in 1970 to 11.7 in 1998 (OFDT, 2002). Daily use of alcohol decreased from 23 percent of adults in 1995 to 15 percent in 2005 (Beck, 2006). Daily use in 1998 was greater in men (31.3%) than in women (12.5%). Daily use of alcohol increased with age from 10 percent at age 30 to 32 percent at age 40, 41 percent at age 50, and 60 percent at age 60 and above. Problematic drinking (risky drinking or dependence) was found in 8.3 percent of adults in 1995 and 8.9 percent in 1999. The rate of problematic drinking in men increased with age from 9.3 percent at age 20 to 19.4 percent at age 50 and then decreased, although it is not known to what extent this is an aging effect or a group effect (OFDT, 2002). The percentage of risky drinking (i.e. excessive drinking without dependence) declined from 30 percent of drinkers at age 20 to 10 percent at age 60, but the percentage of dependent drinkers rose from 2.5 percent at age 20 to 10 percent of drinkers at age 60 (Beck, 2006). First use of alcohol begins on average at 13 years of age. By age 16, 84 percent of boys and 83 percent of girls had experimented with alcohol.

Tobacco. Sales of cigarettes have decreased steadily from about 100 billion units in 1990 to about 55 billion in 2004 and remained stable until 2006 (OFDT, 2006). The value of these sales increased from 6.4 billion euros in 1991 to 13.4 billion in 2007 despite the decrease in volume of sales; this was due to a marked increase in the price of cigarettes. Among adults, 30 percent of men and 23 percent of women smoked daily in 2005 (Beck, 2006). Use of tobacco decreased steadily among adult men from 60 percent in 1970 to about 40 percent in 2004, whereas in women, it moved from 28 percent in 1970 to about 35 percent in 1980 and back to 28 percent in 2004 (Beck, 2006). In 2005, 34 percent of boys and 43 percent of girls aged 17 reported daily use of tobacco, and one-third of them already showed evidence of tobacco addiction.

Cannabis. Cannabis use increased markedly among youths. The percentage of 17-year-old boys who experimented with cannabis rose from 24.7 percent in 1993 to 52.3 percent in 2003 and remained stationary until 2005, whereas that of 17-year-old girls rose from 17.2 percent in 1993 to 47.2 percent in 2003. Regular use of cannabis (more than 10 days a month) remained close to 15 percent among 17-year-old boys and 5 to 6 percent in 17-year-old girls from 2000 to 2005. Cannabis is used chiefly by the younger generations. Its yearly prevalence decreases steadily to 8 percent of men and 3 percent of women by age 40 and lower still later (Beck, 2006).

Other Drugs. Experimentation with cocaine, amphetamine, and heroin by percentage of the population ages 28 to 44 was 1.3, 1.0, and less than 0.1, respectively in 1992; it rose to 3.5, 3.0, and 1.8, respectively in 2005. Yearly use in 2005 for ages 18 to 25 was 1.5 for cocaine, 1.4 for Ecstasy, 0.8 for hallucinogenic mushrooms, 0.5

for solvents, 0.4 for LSD, 0.4 for heroin, and 0.3 for amphetamines (Beck, 2006). In 2005 psychotropic medications were used during the past year by 24 percent of women and 14 percent of men. Lowest use was among the 18 to 25 age group, with 15 percent of women and 9 percent of the men using them during the previous year. Frequency of use increased with age until ages 45 to 54 and remained steady thereafter (Beck, 2006).

POLYCONSUMPTION

The levels of polyconsumption are: (a) polyexperimentation; (b) repeated polyconsumption; (c) polyconsumption at the same occasion; and (d) polydependency. Among the general adult population 18 to 44 years of age, people who used cannabis had an average polyexperimentation of 1.4 drugs. For those who used heroin, the average polyexperimentation was 4.7 drugs; for the rest it varied between 3.8 and 4.2. With regard to repeated polyconsumption, only alcohol, tobacco, and cannabis had enough subjects to get reliable data. In the population ages 18 to 44, 9.6 percent used alcohol and tobacco; 3.4 percent used tobacco and cannabis; 1.7 percent used alcohol, tobacco, and cannabis; and 0.4 percent used alcohol and cannabis. (OFDT, 2002). Among adolescents aged 17 in 2000, those who used cannabis experimented with 1.4 other drugs (not including alcohol and tobacco), those using psychotropic medications experimented with 1.7 percent other drugs, and those who used heroin, LSD, amphetamines, or cocaine experimented with more than five drugs. A relatively small number of adolescents used two or more drugs at the same occasion for one of the following purposes: to maximize the effects, to correct the effects of one drug with another to obtain the optimal combination, to master the negative effects following the first drug, or because there was not enough of one type of drug (OFDT, 2002).

GOVERNMENTAL POLICY

French government policies are based on laws that are implemented by specific ministries or agencies. Ministries use *décrets* that entail an obligation (analogous to regulations in the U.S.) and *ciculaires* that are advisory (analogous to guidelines in the U.S., but somewhat stronger). The actual effect of the law depends not only upon the strength of the provisions in the law but also on the manner in which it is implemented through *décrets* and *circulaires*, and through the penalties for violations. The interval of time between enactment of a law and implementation is also an important variable.

ALCOHOL LEGISLATION

The objects of policies are to limit harmful effects, to decrease the total use of alcohol in the population, and to delay the age when youth start drinking. Gradual approaches are used because use of alcohol is ingrained in the culture and because of the importance of the alcohol industry to the economy and its political power.

Efforts to decrease car accidents when the drivers are under the influence of alcohol led to the first definition of legal alcohol levels of 0.4 grams per liter of exhaled air and 0.8 grams per liter of blood in the law of July 8, 1970. Subsequent laws increased the penalties for driving under the influence and lowered the legal blood limit to 0.5 grams per liter in 1990.

The Barzarch law of July 10, 1987, targeted advertising and other means of publicizing alcohol products. It prohibited television advertising and alcohol companies' sponsorship of sports events. It was ineffective as the industry found ways of getting around the law. A stronger law was passed on January 10, 1991. It is named the loi Evin, after the minister of health Claude Evin. It prohibits direct or indirect advertising or sponsorship of public events, with specified exceptions. It also mandates statements about health dangers of alcohol on product labels. It sets relatively high fines on infractions of these rules, up to 100,000 euros. It has encountered opposition both within France and in Europe, but the government has been steady in implementing it over a number of years.

TOBACCO

The production and sale of tobacco was for a long time a state monopoly that provided an important source of revenue. It was privatized in 1995, but it remains an important source of tax funds. Tobacco, an addictive substance, is an ingrained habit among much of the French public. The Veil law of July 9, 1976, allowed publicity only in the press, forbid sponsorship of sports events, required a message about health risks on the package, and forbade smoking in public places when it posed a health

hazard for others. The law was ineffective, and both advertising and sponsorship expenses increased in the following decade.

The Evin law of January 10, 1991 (Logifrance, 1991) took up the challenge. It prohibited advertising and other publicity except for certain specified sites and increased the fine for violations; it prohibited smoking in public places; it maintained messages about health risks on product labels and set significant fines (e.g. 5,000 francs for the smoker); and it removed tobacco from the national price index, thus facilitating a rise in the cost of cigarettes. However, it was implemented very gradually; for instance, restaurants were allowed to have a smoking section until December 31, 2007, and only in 2008, 17 years after passage of the law, did restaurants become totally smoke free.

ILLICIT DRUGS PHASE 1: LAW OF 1970

The problem of illicit drug use became pressing in France in the 1960s when an increasing number of French youths started to use these substances. The government's response was initially repressive. The law of December 31, 1970, set the use of heroin and other drugs, such as cocaine and cannabis, as an infraction punishable by jail time. However, an arrestee may escape a jail sentence through treatment with a psychiatrist with the goal of becoming drug free. At that time French professionals and policy makers saw the problem of drug addiction as an individual's own problem, a deviation for which that person needed treatment. This contrasts with the social approach to the problem that developed at the same time in the Netherlands There, the addict was conceptualized as a marginalized person, living in a state of social misery, and management allowed the use of morphine or other opium derivatives, along with helping to reintegrate the individual into society (Van Solinge, 1996).

French opposition to this approach was slow in developing. There was a small effort to develop methadone substitution programs on an experimental basis, sponsored by Institut National de la Santé et de la Recherche Médicale (INSERM) that led to two programs for 20 people each in 1973. They were not followed up by other programs, however, as the opinion of politicians as well as professionals was strongly against substitution for nearly two decades, so psychiatry maintained a monopoly on treatment (Augé-Caumon et al., 2002).

However, a more important opposition developed in the 1980s, stimulated in part by the HIV/AIDS epidemic among drug users. In the 1980s, 30 percent of heroin addicts tested sero-positive for HIV and 60 percent for hepatitis B or C. Associations that included consumers and professionals organized to "limit the damage or reduce harm" (Van Solinge, 1996). Individuals engaged in auto-substitution therapy with opium derivatives available without prescription, including derivatives of codeine (Augé-Caumon, 2002). Several primary care physicians led by Jean Carpentier treated heroin addicts with morphine sulfate (Van Solinge, 1996) and with buprenorphine that had been developed by Schering-Plough. (Augé-Caumon, 2002).

PHASE 2: *DÉCRET* AND *CIRCULAIRES*

The new phase did not start with a new law, but rather with the *décret* of June 29, 1992, which established the Centres Spécialisés de Soins aux Toxicomanes (CSST), with a mission not only for psychiatric care, but also for social and educative functions to help patients during the period of withdrawal and give social support in the familial environment. There was no mention of methadone substitution in that *décret.* However, within a year the minister of health issued two *circulaires* (1993 and 1994) that set the CSSTs as methadone-substitution sites in large cities of France, with strict standards for eligibility to the treatment (including duration of heroin dependency of at least five years), for control of utilization and storing of methadone, and for services offered (Augé-Caumon, 2002). The number of patients rose from 53 in 1993 to more than 1000 in 1995 (Van Selinge, 1996). A third *circulaire* in 1995 deleted the requirement for a five-year previous period of dependency. Finally, a fourth *circulaire* in 1995 set up the present system of substitution treatment. Methadone could be initiated only in specialized centers, but the treatment could be continued by the patient's physician. High-dose buprenorphine was also approved for substitution, and it could be prescribed by primary care physicians. By 2001, 12,000 persons were treated with methadone, and 80,000 persons were treated with buprenorphine (Augé-Caumont, 2002).

PHASE 3: MONITORING AND EVALUATION

By 2007, Centres d'Évaluation et d'Information sur la Pharmacodépendence (CEIP) had been

organized in 11 large cities (Bordeaux, Caen, Grenoble, Lille, Lyon, Marseille, Montpellier, Nancy, Nantes, Paris, and Toulouse). Their functions are (a) to develop statistics on pharmacodependence or abuse of drugs and evaluate the addicting potential of new illicit drugs or pharmaceuticals; (b) to inform professionals, the public, and policy makers about the risks of pharmacodependence and drug abuse by responding to queries or through bulletins or meetings; and (c) to do research, including animal experimentation and human surveys, to study toxicity and addictive potential of new drugs or substances.

The CEIPS utilize several tools to fulfill their functions:

- The OPPIDUM (Observatoire des Produits Psychotropes Illicites ou Détournés de leur Utilisation Médicamenteuse) does yearly surveys of patients in substitution therapy or with a diagnosis of pharmacodependence in health facilities. In 2006, it followed 3,867 patients and 7,737 prescriptions.
- OSIAP (Ordonnances Suspectes Indications d'Abus Possible) is a network of sentinel pharmacists attached to each CEIP. In 2006 it identified 314 prescriptions involving 514 medications.
- SINTES (Système d'Identification National des Toxicants et des Substances) is a social and health partnership to identify new substances or changes in degree of toxicity of substances, based on studies conducted in relation to social events or "rave parties."
- Enquête ASOS (Analgésiques, Stupéfiants, et Ordonnaces Sécuritées) is a survey of 800 pharmacies for utilization of analgesic, sedative, or other restricted drugs.
- Enquête Soumission Chimique investigates reported cases of people who were given drugs without being aware of it at parties or other occasions, usually to perform sexual or other acts on them (chemical submission).
- DRAMES (Décès en Rellation avec l'Abus de Médications et de Substances) reports on postmortem studies by toxicology laboratories on drug addicts suspected of dying from overdoses. It conducted studies on 177 postmortems in 2006.

Coordination and Information Transfer. Each of the above studies is administered by one CEIP (for instance, OPPIDUM is administered by a CEIP in Marseille) that integrates the results to present a national evaluation. The material collected by the CEIP is presented to and evaluated by the Commission Nationale des Stupéfiants et des Psychotropes (CNSP) which, in turn, transmits its findings and advice to the Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSPS). The AFSSPS has a broader mission over all health products and drugs (somewhat similar to the Food Drug Administration of the United States). It also exchanges information with a parallel system of data on drugs, the Observatoire Francais des Drogues et des Toxicomanes (OFDT).

The ministry of health requests and receives information and advice from the CNSP and the AFSSPS. The AFSSPS communicates with the European Medication Agency (EMEA) and the European Observatory of Drugs and Toxic substances (EODT) and the WHO (World Health Organization) Expert Committee on Pharmacodependence.

The CEIPs also serve as a source of local information for health facilities and health professionals. In turn, they receive spontaneous notifications of drug abuse from physicians, pharmacists, and other health professionals and often perform studies based on such local notifications.

CONCLUSION

The French government's initial punitive approach to illicit drugs use (imprisonment or injunction to psychiatric treatment) in the 1970s has evolved since the 1990s into a more comprehensive and socially-oriented approach. The development of methadone therapy, although late in comparison to other countries, has proceeded rapidly and is now well established, along with a pharmaceutical alternative administered by primary care physicians. The comprehensive approach developed by the CEIP may pave the way for a more socially-oriented approach to illicit drug use, as opposed to a punitive one. However, except for the success of replacement therapy, the fight against illicit drugs has not yet progressed to the point of decreasing use of these drugs in the population. This is in contrast to the success of the steady gradual methods that have led to the decreased prevalence of alcohol use in the

adult population and the decreased use of tobacco by men and, following an earlier increase, by women.

The main problem with alcohol and tobacco as well as illicit drugs concerns the adolescent generation. Education about tobacco in schools from the earliest to the final grade levels is a promising approach that might also work for alcohol. Cannabis represents a special problem because a vast majority of adolescents as well as a significant part of the adult population do not consider it a dangerous drug, and it is now well implanted. France may have to consider a legalization of cannabis complemented by strong regulation and extensive education and surveillance of youth for psychosocial complications of its use. In addition, the problem of the marginalized population, major drug users, must be addressed in dealing not only with drugs, but by the related problems of low income, high levels of unemployment or underemployment, and lack of integration into society.

See also **Alcohol; Amphetamine; Cannabis Sativa; Cocaine; Crack; European Union; Foreign Policy and Drugs, United States; Germany; Hallucinogens; Heroin; International Control Policies; International Drug Supply Systems; Italy; Lysergic Acid Diethylamide (LSD) and Psychedelics; Methadone Maintenance Programs; Netherlands; Opiates/Opioids; Opium: International Overview; Polydrug Abuse; Psychoactive; Rave; Spain; Substance Abuse and AIDS; Tobacco: Dependence; Treatment, Pharmacological Approaches to: Buprenorphine; Treatment, Pharmacological Approaches to: Methadone; World Health Organization Expert Committee on Drug Dependence.**

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FREEBASING. The illicit practice of smoking cocaine is generally referred to as freebasing. The hydrochloride form of cocaine (powder) is highly soluble in water and, therefore, is efficiently absorbed by the mucous membranes when taken intranasally (snorted) or via blood when injected intravenously (shot up). This form of cocaine is, however, destroyed

when it is heated to the temperatures required for smoking it. Therefore, the cocaine alkaloid, called *crack* or *freebase*, is the form that is smoked. Although not always differentiated, freebase actually refers to cocaine in the base state with all the adulterants removed (Inciardi, 1991). Cocaine hydrochloride is combined with an alkaline substance, such as sodium hydroxide or ammonia, to remove the hydrochloride. The *free* cocaine *base* is then dissolved in ether, and pure cocaine-base crystals are formed. It has been estimated that approximately 560 milligrams of cocaine freebase can be extracted from one gram of street cocaine hydrochloride (Siegel, 1982). Cocaine freebase has a melting point of 208°F (98°C) and is volatile at temperatures above 194°F (90°C), therefore providing an active drug for smoking. Crack, in contrast, although also in the base state and used for smoking (or freebasing), does not have the adulterants of the street cocaine removed. Cocaine base is soluble in alcohol, acetone, oils, and ether—but is almost insoluble in water.

Cocaine freebase is usually smoked in a water pipe containing fine mesh screens, which trap the heated cocaine as it melts. A temperature of 200°F (93°C) is the most efficient. Although the amount of cocaine absorbed by the smoker varies—depending on the kind of pipe used, the temperature of the heat source, and the inhalation pattern of the user—under optimal conditions approximately 30 to 35 percent of the cocaine placed on the mesh screen is absorbed by the smoker.

COMPARISON OF COCAINE AND METHAMPHETAMINE SMOKING

Vapor inhalation of the (+) isomer of methamphetamine hydrochloride, colloquially known as *ice* has several differences when compared to vapor inhalation of cocaine freebase. Although both methamphetamine and cocaine freebase have their origin as a salt, cocaine hydrochloride must be pretreated with an alkaline substance to remove the hydrochloride, thus creating the freebase of cocaine that can be heated and inhaled as vapor. In contrast, methamphetamine hydrochloride can be heated and inhaled without adulterating the original compound.

When heated, cocaine freebase has a melting temperature of 208°F while methamphetamine hydrochloride melts at 268°F. Once the appropriate melting temperature is met for each substance, vapors will form and can be inhaled. Significant amounts of cocaine freebase vapor are lost through pyrolysis (chemical change caused by heat) and little condensation appears on the water pipe, suggesting decreased amounts of inhaled vapor. Methamphetamine hydrochloride, however, condenses as a crystalline solid on the cooler areas of the glass pipe. It is thought that this same phenomenon occurs in the mouth and throat of the user, leading to rapid methamphetamine absorption through the lungs as well as delayed absorption through the oral mucosa.

These differences in drug absorption have been demonstrated by comparisons of plasma levels of cocaine and methamphetamine after smoking the individual substances. Plasma levels of cocaine peak and decline rapidly, with a half-life of approximately forty-five to sixty minutes. Methamphetamine plasma levels also rise rapidly, but the half-life is approximately eight to twelve hours. The delayed absorption of methamphetamine from the oral mucosa is thought to play a role in the extended half-life. Differences in the metabolism of cocaine and methamphetamine also contribute to the disparity in plasma half-life. Cocaine is quickly degraded to inactive metabolites by plasma esterases (enzymes) and cleared from the bloodstream. Methamphetamine is eliminated by enzymes with limited plasma distribution and limited activity and, unlike cocaine, is converted to active metabolites that prolong the action of the drug. These active metabolites can accumulate, and repeated smoking of methamphetamine and its active metabolites can lead to dangerous levels of methamphetamine in the plasma.

In summary, differences between cocaine freebase vapor inhalation and methamphetamine hydrochloride inhalation include method of preparing the substance, melting temperature, metabolism, and length of plasma half-life. These differences can have important clinical implications. For example, methamphetamine can cause paranoid symptoms that last considerably longer than those ordinarily seen after cocaine smoking. Distinguishing between drug-induced paranoia and other causes of paranoia thus requires a different length of drug-free observation depending on which drug was inhaled. Understanding the differences between cocaine freebase inhalation and methamphetamine inhalation, particularly the difference in duration of action of the two drugs, can be important in the evaluation and management of patients with stimulant abuse.

Although in use since the mid-1970s, freebasing cocaine became popular in the United States in the early 1980s. The popularity of this route of administration was responsible for the rise in U.S. cocaine use during the mid-1980s. When cocaine is smoked, it is rapidly absorbed and reaches the brain within a few seconds. Thus, users get a substantial immediate rush and an almost instant "high," comparable to that after intravenous cocaine. This is in contrast to intranasal use of cocaine, which engenders a high with a much slower onset. Freebasing is thus a convenient way of taking cocaine, with the possibility of repeated and substantial doses. Since the likelihood of abuse is related to the rapidity with which a drug reaches the brain, smoking cocaine makes it more likely that use will lead to abuse than does snorting the drug. Despite losses of more than half of the cocaine when it is smoked, sufficient cocaine rapidly reaches the brain, providing an intense drug effect—which users repeat, often to toxicity. The danger of freebasing, in addition to the inherent danger of cocaine use, lies in what some users perceive to be the greater social acceptability of a route of administration that requires minimal paraphernalia and can achieve toxic levels of cocaine with relative ease.

See also **Amphetamine Epidemics, International; Coca Paste; Complications: Cardiovascular System (Alcohol and Cocaine); Methamphetamine; Pharmacokinetics: General.**

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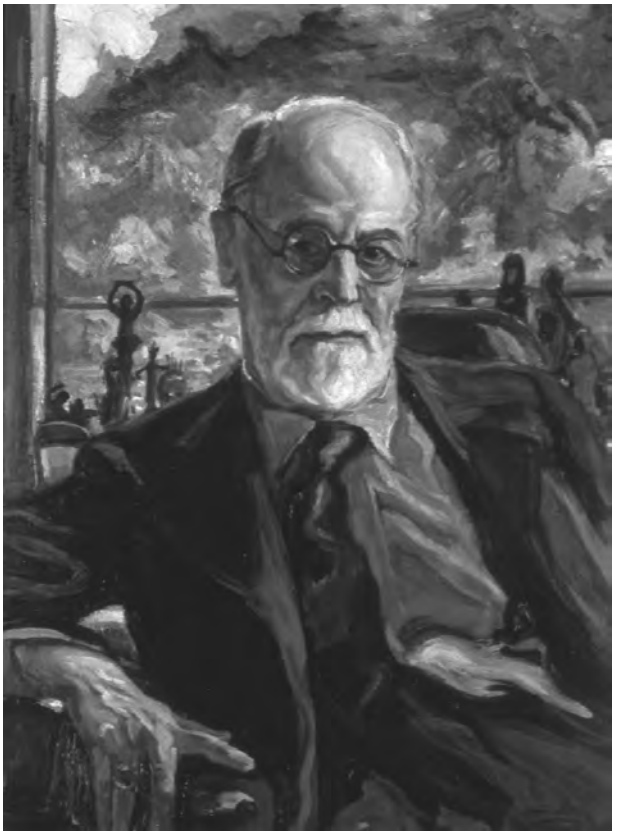
FREUD AND COCAINE. Sigmund Freud (1856–1939), Austrian neurologist and founder of psychoanalysis, became interested in cocaine in 1884. The following year (1885) he published "Contribution to the Knowledge of the Effect of Cocaine." At the time he was in his late twenties and was a medical house officer at the Vienna hospital, Allgemeine Krankenhaus. He was able both to gain access to the literature about cocaine and, at some expense, to the substance itself (which was not illegal at that time). In a letter to his fiancée Martha Bernays, Freud referred to the role cocaine played in the discovery of his medical vocation. Freud indicated that he wanted to medically cure patients from their suffering, and he hoped he had found a panacea in the form of cocaine. (There had been articles in the U.S. medical literature describing cocaine used in the treatment of various ills and for drug dependencies as a panacea.)

Freud noticed the ability of cocaine to fend off fatigue and enhance mood. He was particularly taken by suggestions that cocaine might be an adjunct to, or even a cure for, alcohol or opioid dependencies. His interest was heightened because one of his teachers and close friends, Ernst von Fleischl-Marxow, had become an opiate addict. Using cocaine, Freud treated him with almost disastrous results. At the time, there was no opprobrium attached to the use of cocaine and relatively little concern about any adverse effects.

Freud performed a number of cocaine experiments on himself and reported the results in the aforementioned experimental paper, "Contribution to Knowledge of the Effects of Cocaine." These were reasonable studies that provided useful data about the physiological and psychological effects of cocaine. Freud mentioned that individuals react differently to the drug. Biographies of Freud, such as Ernest



Freud had hoped to use cocaine to medically treat patients suffering from mood disorders or fatigue. THE LIBRARY OF CONGRESS.

Jones's *The Life and Work of Sigmund Freud*, have tended to disparage his experimental paper and other works on cocaine. Although his work was done on himself and was limited in its scope, it has been confirmed in modern replications. Freud was initially skeptical about the possible addictive properties of cocaine in normal individuals, but later, in the face of evidence and criticism, he was less vehement on the subject. He became, in later life, very sensitive to criticism of his earlier views on cocaine.

From 1884 to 1887 Freud wrote four papers concerning cocaine, including a definitive review in 1884. In the last of his cocaine papers, "Craving for and Fear of Cocaine" (1887), Freud wrote that cocaine affected people in different ways; it had become an unpredictable object, and it was not possible to know who would have a general reaction to it. Regarding addiction, Freud's so-called cocaine episode demonstrates two related and crucial aspects of his thought on the subject: First, the ultimate cause of addiction is not situated in the drug but in the individual predisposition of the user; and second, drugs have effects that are particular because they are dependent on the constitution of the user. He obviously felt comfortable in both taking cocaine and writing about it in his letters. He mentions and discusses his use of and dreams about cocaine in the *Interpretation of Dreams* (1889). The true extent and duration of his self-experiments is not known, since access to his correspondence has been severely restricted.

Freud is sometimes credited with the discovery of local anesthesia because of his proposal in his cocaine review paper that the substance could be used for this purpose. He also claims suggesting the idea to both Koenigstein and Carl Koller prior to their experiments in ophthalmology, which led to the initial papers on local or topical anesthesia. There is a semantic problem in understanding these claims. Almost all investigators of cocaine had noticed the numbing properties of the drug when placed on the tongue. The idea that this property had a practical use in ophthalmological surgery does belong to Carl Koller, a friend and colleague of Freud, who did the proper experiments and published them promptly. The controversy about the discovery between Koller and Koenigstein with Freud's mediation is well covered in the article by Hortense Koller Becker, "Carl Koller and Cocaine," in *Psychoanalytic Quarterly* (1963).

Extreme viewpoints that attribute Freud's behavior and writings to the influence of the toxic effects of cocaine are unsubstantiated by evidence. Clearly, he used cocaine as a psychotropic agent on himself, and this experience led to his faith in its relative safety. Despite these facts, there is no real support for a viewpoint that he was an addict or that his thought was markedly affected by his drug usage. The combined notoriety of both Freud and cocaine has led to speculative exaggerations that make better newspaper headlines than history.

See also **Cocaine; Psychoanalysis.**

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FUNDING AND SERVICE DELIVERY OF TREATMENT.

There is no single best method or setting for the treatment of substance abuse disorders. Treatment is offered in specialty units of general and psychiatric hospitals, residential facilities, halfway houses, outpatient clinics, mental health centers, jails and prisons, general medical practitioners' offices (e.g., family physician, pediatrician), collaborative-care settings, and the offices of private practitioners. (Collaborative care involves settings in which case management and a multidisciplinary consultation between the case manager, the primary care provider, and a consulting psychiatrist are central to the care of the individual; this type of setting is particularly effective for the treatment of depression.) Since the 1970s, there has been significant progress in the movement to unify the treatment of substance abuse and mental health disorders under the banner of "behavioral health service delivery." There has also been a recognition that substance abuse and mental health disorders occur together in many individuals, who are said to be suffering from "co-occurring disorders." In the United States during the 1970s and 1980s, persons with disorders of drug abuse or dependency were commonly treated in programs completely separate from those programs serving persons with alcohol abuse or dependency. By the late 1980s and early 1990s, however, the two treatment systems were merged in most areas across the country.

TREATMENT COSTS

The cost of substance abuse treatment and substance dependence treatment vary greatly depending on the setting. During the first decade of the twenty-first century, the annual national cost estimate for nonhospital residential substance abuse treatment in a specialty setting (the most expensive form of service delivery for this population) was around $62 per patient per day, with an overall annual cost of $2.3 billion. For outpatient nonmethadone treatment in a specialty treatment setting, the cost per patient per day was about $10, with an annual cost estimate of $2.7 billion. For methadone maintenance in specialty settings, the cost was just over $9 per day per patient, with an annual cost of $0.6 billion. In total, the cost of substance abuse treatment in a specialty setting was about $5.5 billion per year, with nonhospital residential admissions costing about $2.2 billion, outpatient methadone clinic services costing around $800,000, and outpatient nonmethadone treatment costing $2.5 billion. Roughly 100,000 people were served in around 50 nonhospital residential specialty settings, 152,000 were served in 44 outpatient methadone clinics, and 807,000 were served in 222 nonmethadone outpatient specialty settings.

Within the outpatient settings, the average cost per visit was significantly lower for methadone clinic visits ($14.50, with a reported range of $7.82 to $58.81) than for nonmethadone outpatient facilities (about $22, with a reported range of $4.43 to $204.13). On average, the cost for an inpatient nonhospital residential admission was about $3,000, with a range of $308 to $18,482. The cost per admission for outpatient methadone treatment was around $6,000, with a range of $2,109 to $32,630, and the cost of nonmethadone outpatient treatment was just over $1,100, with a range of $188 to $12,650. The total cost for all treatment types was $5.5 billion, or $1,900 per admission, with around 3 million people receiving services. Inpatient programs, although they are the most costly, are generally of the shortest duration, averaging around 30 days. Outpatient programs vary in duration from a few months to several years or more.

At the beginning of the twenty-first century, behavioral health treatments in the United States (substance abuse and mental health services

combined) cost $104 billion, putting them among the top fifteen health-care areas in terms of expenditures. Eighteen billion dollars, or 18 percent of the total, was spent on substance abuse treatment. These figures do not take into account the significant percentage of substance abuse and behavioral health services provided in general medical settings by health care professionals who are not behavioral health specialists, nor do they consider the cost of medications used in the treatment of behavioral disorders.

PRIVATE HEALTH INSURANCE

The availability of private health-insurance coverage for substance abuse treatment began to grow exponentially in the 1980s. By the first decade of the twenty-first century, more than 98 percent of health insurance plans had explicit coverage for behavioral health services. Individuals with private insurance have a greater range of treatment providers to choose from than those who are indigent and have only government-funded programs at their disposal. Programs that mainly rely on insurance reimbursement, however, tend to be more expensive than those that receive the bulk of their support from government sources. Private insurance pays about 20 percent of the overall costs for behavioral health treatment annually.

U.S. GOVERNMENT FINANCING

In the general health care system (medical and behavioral health combined) in the United States, about 70 percent of the cost of services is borne by the individual, an insurance company, or some other private third-party payer. For substance abuse or mental health care, in contrast, the government (public health services) supplies nearly 70 percent of the funds for treatment.

States often finance treatment by reimbursing providers through public-welfare programs, local public health facilities, or through grants and contracts. Some states transfer funds to county and local governments, which, in turn, purchase services from providers. Another financing mechanism is Medicaid, a combined state and federal program that pays medical bills for low-income persons. Under Medicaid, states can pay for substance abuse care in inpatient general hospitals, clinics, outpatient hospital and rehabilitation services, and group homes with sixteen or fewer beds.

Medicare is a federal program that pays the health-care costs of persons 65 years of age or older and those who are disabled. For individuals with substance abuse disorders, this program primarily covers inpatient hospital treatment of alcohol or drug abuse, as well as some medically necessary services in outpatient settings. The primary federal mechanism for paying for alcohol and drug treatment is the Substance Abuse Prevention and Treatment (SAPT) Block Grant, administered by the Department of Health and Human Services. Funds from the block grant are distributed to the states (and territories) using a formula that takes the characteristics of each state's population into account. In fiscal year 2009, Congress appropriated approximately $1.7 billion for the SAPT Block Grant, per the 2009 Health and Human Service Budget Appropriations request. The federal government also makes grants to individual treatment providers to support innovative treatment approaches, improve the quality of treatment, or ensure services are available for underserved or special populations.

See also **U.S. Government Agencies.**

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GAMBLING. The formal group of impulse control disorders (ICDs) in the *Diagnostic and Statistical Manual Fourth Edition Text Revision* (*DSM-IV-TR*) is termed *ICDs Not Elsewhere Classified* and includes pathological gambling (PG), intermittent explosive disorder, kleptomania, pyromania, trichotillomania, and ICDs not otherwise specified. The ICDs are described as a heterogeneous cluster of disorders linked by a "failure to resist," impulses to engage in harmful, disturbing or distressing behaviors (p. 663). PG is the ICD that, as of 2008, has been most widely studied. PG and other ICDs have been conceptualized both as *obsessive-compulsive spectrum disorders* and *behavioral addictions*. Consistent with the latter formulation, ICDs are considered to have a core set of clinical features, including the following: (1) compulsive and repetitive performance of the problematic behavior despite adverse consequences; (2) loss of control over the behavior; (3) an appetitive urge or *craving* state before starting the behavior; and (4) a pleasurable quality associated with its performance. As an example, individuals with PG "often increase the frequency of their bets or the amount of money gambled in order to achieve the desired level of excitement," suggestive of tolerance (Dell'Osso et al., 2005, p. 2).

With emphasis on its impulsive characteristics, PG can be thought of as an obsessive-compulsive spectrum disorder, in which affected individuals experience an intense unpleasantness resulting in an attendant neurophysiological compensation, which promotes an intense drive to perform a specific behavior. The model for PG as a non-substance related addiction is supported by the frequent co-occurrence of PG and substance use disorders (SUDs), whereas there is less consistent evidence of comorbidity between PG and OCD. Because depression and suicidality, as well as impaired judgment (suggestive of bipolar disorder) are seen at a rate greater than chance among individuals with PG, it has been proposed that PG is an affective spectrum disorder (Dell'Osso et al., 2005, p. 2).

CHARACTERIZATION, CLINICAL COURSE, AND PREVALENCE

PG is characterized by persistent and recurrent maladaptive patterns of gambling behavior and is associated with impaired functioning, reduced quality of life, and a high frequency of bankruptcy, divorce, and incarceration. PG usually begins in adolescence or early adulthood, with males tending to start at an earlier age. Although prospective studies are largely lacking, PG appears to follow a similar trajectory as substance dependence, with high prevalence rates among adolescents and young adults and lower rates in older adults, along with periods of abstinence and relapse. Other phenomenological similarities exist between PG and SUDs, such as a *telescoping* pattern in women that signifies a foreshortened timeframe between age at onset of the behavior and the development of a problem relative to the course seen in men.

Treatment interventions are common to PG and SUDs. For example, the opioid antagonist

naltrexone, a drug that is approved by the U.S. Food and Drug Administration for the treatment of alcohol dependence and opiate dependence, has also been found in placebo-controlled trials to be helpful in the treatment of PG. In alcohol dependence, naltrexone appears particularly linked to reduced alcohol cravings and heavy drinking. Analogously, naltrexone appears particularly helpful for individuals with strong gambling urges. Other approaches (e.g., behavioral therapies such as motivational enhancement and cognitive behavioral therapy) that have been found to be effective in the treatment of SUDs also appear helpful in PG. Twelve-step programs initially developed to deal with alcohol and other SUDs (e.g., Alcoholics Anonymous) have been widely used for PG (e.g., Gambler's Anonymous).

In comparison to other psychiatric disorders, the pathophysiology of PG is poorly understood. Until shortly before 2008, PG had been excluded from many major psychiatric epidemiological surveys, such as the National Comorbidity Survey. PG and other ICDs have historically been excluded from widely used structured clinical instruments used to diagnose psychiatric disorders. This latter point is important because the under-diagnosis and treatment of PG and other ICDs are suggested by some studies indicating high frequencies of these disorders co-occurring with other psychiatric disorders. One study found that over 30 percent of 204 hospitalized psychiatric inpatients had a current ICD, compared to less than 2 percent who were diagnosed with such a disorder at the time of their initial hospital admission. Improved identification and treatment of ICDs could be facilitated by brief screening instruments because the lack of efficient screening mechanisms may put these patients at risk for worse treatment outcomes.

DEFINING ADDICTION

The concept of addiction has changed over time. One view is that addictions result from one's genetic predisposition and access to the specific reward stimulus that signals a cue for the addictive behavior (for example, an individual with PG having free access to casinos). A key component of addiction is diminished *behavioral control*, which leads to behaviors *in the service of the addiction*; behaviors that are performed despite anticipated, longer term adverse consequences. This diminished behavioral control does not always occur in individuals who develop tolerance to a particular drug. An example involves the development of physiological (physical) tolerance while taking a prescribed medication (for example, a beta-blocker used in the treatment of heart disease). Chronic administration may lead to tolerance, physical dependence, and withdrawal upon immediate cessation of the drug. However, use of the drug is generally not associated with addiction (i.e., drug-seeking behavior and drug use that interferes with major areas of life functioning).

TOWARD A MODEL OF ADDICTION, IMPULSIVITY, AND PATHOLOGICAL GAMBLING

The core clinical features of addiction overlap with a definition proposed for impulsivity that emphasizes "a predisposition toward rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequence of these reactions to the impulsive individual or others" (Moeller et al., 2001, p. 1784). PG has been described as a *behavioral addiction* or an *addiction without the drug* because of shared similar features with substance dependence. A strong connection between addiction and the impulsive behavior seen in PG is highlighted in the proposed Reward Deficiency Syndrome model, which suggests that diminished dopamine (DA) function in brain reward pathways places vulnerable individuals at risk for addictive, impulsive, and compulsive behaviors. Similar models postulating the relevance of DA reward pathways in individuals vulnerable to drug addiction, excessive eating, and PG are suggested by the "impaired response inhibition and salience attribution" model of addiction (Goldstein & Volkow, 2002, p. 1643) and the addiction development model put forth by Koob and Le Moal (2001). Each of these models incorporates environmental and genetic factors as factors in the development of addictions.

Brain network models of addiction have been proposed to explain both PG and SUDs. These models have focused on neural circuits underlying motivated behaviors and how they may become dysregulated in addictive processes. A fundamental aspect of an evolving addiction is the progressive development of repetitive, habitual behaviors, which rely upon progressive activation of specialized brain

structures; for example, increased usage of upper (dorsal) portions of a subcortical brain structure known as the striatum (consisting of the caudate nucleus and the putamen), as opposed to other, lower (ventral) parts of striatal brain networks. The encoding of such behavior may begin early with the acute rewarding effects of a drug or a stimulating experience and may involve dopamine release and alterations in cellular signaling. Later, changes in brain cellular protein, receptor sub-unit, and enzyme synthesis, may be seen later in the addiction process. Thus, behavior becomes more habitual over time or the associated learned cues become potent in the absence of reward. It is hypothesized that a drug cue or related stimulus leads to heightened motivation for drug-seeking, and this results in craving and addictive behaviors.

NEUROBIOLOGY

The dopamine system influences rewarding and reinforcing behaviors and has been implicated in addictions. Alterations in dopaminergic pathways have been proposed to underlie reward seeking and pleasure in PG and SUDs. Acute ingestion of drugs of abuse increases DA transmission in the basal ganglia, an important biological process for behavioral reinforcement and learned associations encoding addictive behaviors.

Other monoamine systems have been implicated in the pathophysiology of PG and SUDs. Serotonin (5-HT) has been implicated in the initiation and cessation of the problematic behavior and norepinephrine (NE) has been associated with arousal and excitement. These findings are central to hypotheses that underlie the use of medications in the treatment of PG, which are based on the neurobiology of PG and other impulse control disorders. Thus, effective pharmacological treatments can provide insight into the pathophysiology of PG, and vice versa.

ANIMAL MODELS OF IMPULSIVITY AND NEURONAL ACTIVATION

Animal models of impulsivity, specifically those designed to assess levels of motor activity, lack of impulse control, and impulsive decision making have been developed. Some of these models involve choice preference paradigms that include the simultaneous assessment of real-time neurophysiological and neurochemical measures. This experimental approach has been used as a means of mapping impulsive behavior (e.g., deficits in impulse regulation under stress) onto specific brain circuitry. It has been suggested that upper and lower cortical brain regions represent distinct areas of impulsive behavior which carry unique brain chemicals transmitting signals that are separately regulated. In particular, discrete areas of frontal cortex have been divided into functionally "dissociable areas," whose distinctive brain chemistries could reflect the divergence of serotonin and dopamine signal modulation implicated in impulsive choice (Winstanley et al., 2006, p. 112).

GENETIC CONSIDERATIONS

Data from twin studies suggest that a substantial degree of the risk for PG is heritable. Shah and colleagues determined that the prevalence of PG in the Vietnam Era Twin Registry was 1.4 percent. Of twins reporting gambling at least twenty-five times in a year in their lifetime, 29 percent (7.6% of the total cohort) also reported at least one symptom of PG. Subsequent investigations of the same sample indicate that genetic and environmental factors contribute to PG, and that overlap exists in the genetic and environmental contributions between PG and alcohol dependence and PG and adult antisocial behaviors. In addition, the majority of the co-occurrence between PG and major depression appears to be determined by common genetic factors. Thus, environmental and intrinsic genetic factors contribute to vulnerability to both PG and substance abuse. An increased prevalence of these disorders is seen within families and across generations and is determined by the genetic variance in risk for substance addiction (estimated to be approximately 60%) and in the liability for symptomatology in PG (estimated to be between 35% to 54%).

Regarding particular molecular genetic mechanisms, specific variants of serotonergic and dopaminergic genes have been implicated in preliminary studies of PG. The genes implicated include those coding for monamine oxidase A (MAO-A), the serotonin transporter, and the D1, D2, and D4 dopamine receptors. Some differences in allelic variation related to PG appear influenced by sex status, raising the possibility that genetic contributions to PG among males and females are different.

It should be noted that findings from genetic association studies should be viewed cautiously, particularly since many have methodological limitations (e.g., lack of definitive diagnoses and stratification by racial/ethnic identity). The extent to which these preliminary findings are substantiated in PG and generalize to other ICDs requires further research. More comprehensive diagnostic evaluations, larger population samples, and genome-wide investigation should provide important data that will help delineate more precisely the genetic underpinnings of PG, other ICDs, and SUDs.

PG shares core features with SUDs, including tolerance, withdrawal, repeated attempts to cut back or stop, and impairment in major areas of life functioning. Further research is needed to understand the molecular and biochemical factors underlying the unique and overlapping behavioral features seen in PG and SUDs. An improved understanding of the neurobiology of these disorders will facilitate clinical advances in their identification, prevention, and treatment.

See also **Addiction: Concepts and Definitions; Addictive Personality and Psychological Tests; Gambling Addiction: Assessment; Gambling Addiction: Epidemiology.**

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GAMBLING ADDICTION: ASSESSMENT.

Although pathological gambling (PG) is associated with adverse functioning and is approximately as prevalent as schizophrenia and bipolar disorder, there is some indication that both clinicians and researchers fail to screen for, diagnose, and properly assess the disorder. This entry describes instruments available as of 2008 for the assessment of PG, and provides information on each instrument's psychometric properties. More detailed information on the gambling screening and assessment instruments can be found in chapter 14 and the appendix section of the book *Pathological Gambling: A Clinical Guide to Treatment* (Grant & Potenza, 2004).

SCREENING AND DIAGNOSTIC INSTRUMENTS: SELF-REPORT MEASURES

South Oaks Gambling Screen (SOGS). The South Oaks Gambling Screen (SOGS) is a twenty-item, self-report screening instrument for PG. The

time frame of the SOGS is based on lifetime gambling activity and does not differentiate pathological gamblers in remission from those actively gambling problematically. The SOGS is scored by summing selected items, with a score of ≥5 indicating probable pathological gambling.

The SOGS has demonstrated excellent internal consistency (alpha=0.97) and one-month test-retest reliability (r=0.71). Validity was examined by correlating the SOGS with counselors' independent assessments (r=0.86), family member assessment (r=0.60), and *DSM-III-R* PG diagnosis (r=0.94). The SOGS was compared to a *DSM-III-R* diagnosis of PG and demonstrated satisfactory overall diagnostic accuracy among Gamblers Anonymous members (98.1 percent), university students (95.3 percent), and hospital employees (99.3 percent).

The SOGS has also demonstrated satisfactory internal consistency and validity for a one-year time frame. Satisfactory internal consistency was demonstrated in general (alpha=0.69) and treatment (alpha=0.86) samples. Satisfactory validity was also observed for the SOGS, as shown by correlation with *DSM-IV* criteria (r=0.77 and r=0.83, in general and treatment samples, respectively).

The SOGS has been further modified to assess the last three months of a person's gambling behavior, for which it demonstrated good internal consistency (alpha=0.83). The three-month version of the SOGS also showed good convergent validity (r=0.79) when correlated with the National Opinion Research Center *DSM-IV* Screen for Gambling Problems (NODS).

The SOGS has shown poorer classification accuracy in the general population. The SOGS overestimated the number of pathological gamblers in the general population compared to *DSM-IV* criteria (sensitivity rate=0.67). It also showed a high false positive rate, such that one-half of the cases identified as probable pathological gamblers by the SOGS did not meet *DSM-IV* criteria for PG.

Gamblers Anonymous Twenty Questions (GA-20). The Gamblers Anonymous twenty questions (GA-20) is a self-report measure for identifying problem gamblers. A score of ≥7 indicates that the respondent is a problem gambler. The GA-20 correlates highly with gambling frequency. The GA-20 has also demonstrated high internal consistency (alpha=0.94) and excellent validity (correlation with the SOGS; r=0.94).

Massachusetts Gambling Screen (MAGS). The Massachusetts Gambling Screen (MAGS) is a fourteen-item (only seven of which are scored), self-report screen for problem gambling among adolescents and adults. The MAGS measures past-year behaviors. The MAGS classifies respondents into non-problem, in-transition, or pathological gamblers using a weighted scoring derived from a discriminant function analysis. The seven-item MAGS scale has demonstrated good internal consistency (alpha=0.84) and validity (r=0.83) as correlated with the total *DSM-IV* score.

DSM-IV-MR *(MR=Multiple Response).* The *DSM-IV-MR* is a ten-item self-report questionnaire based on the 10 *DSM-IV* diagnostic criteria for PG. Most items have four response options: (1) never, (2) once or twice, (3) sometimes, and (4) often. Each item is allocated one point, and scores range from 0 to 10. A score of 3 or 4, including at least one point from criteria 8, 9, or 10, indicates that the respondent is a problem gambler, and an individual receiving a score of 5 or greater is classified as a severe problem gambler. The *DSM-IV-MR* has demonstrated satisfactory internal consistency (alpha=0.79) but lacks validity data.

Lie/Bet Questionnaire. The Lie/Bet Questionnaire is a two-item screen for PG that can be used in a self-report format: (1) "Have you ever had to lie to people important to you about how much you gambled?" and (2) "Have you ever felt the need to bet more and more money?" The Lie/Bet Questionnaire has a sensitivity of 0.99 to 1.00, specificity of 0.85 to 0.91, positive predictive power of 0.78 to 0.92, and negative predictive power of 0.99 to 1.00 in comparing Gamblers Anonymous members and non-problem gambling controls.

Early Intervention Gambling Health Test (EIGHT). The Early Intervention Gambling Health Test (EIGHT) is an eight-item, self-report screening instrument designed for use by general

practitioners. A score of ≥4 indicates possible PG. The EIGHT correlates highly with the SOGS (r=0.83) and shows high sensitivity (0.91), but low specificity (0.50) and positive predictive value (0.59) using a *DSM-IV* diagnosis as a criterion measure.

SCREENING AND DIAGNOSTIC INSTRUMENTS: CLINICIAN-ADMINISTERED MEASURES

Structured Clinical Interview for Pathological Gambling (SCI-PG). The Structured Clinical Interview for Pathological Gambling (SCI-PG) is a clinician-administered, *DSM-IV*-based diagnostic interview that is compatible with the Structured Clinical Interview for *DSM-IV* (SCID). The SCI-PG assesses both the ten inclusion criteria and the exclusionary criterion of PG: "not better accounted for by a Manic Episode." The SCI-PG has demonstrated excellent reliability (r=0.97), validity (correlation with the SOGS; r=078) and classification accuracy (sensitivity=0.88, specificity=1.00, positive predictive value=1.00, and negative predictive value=0.67).

Diagnostic Interview for Gambling Schedule (DIGS). The Diagnostic Interview for Gambling Schedule (DIGS) is a structured clinician-administered interview that includes twenty diagnostic symptom items (lifetime and past-year), gambling treatment history, age of onset of gambling, and family and social functioning. The *DSM-IV* diagnostic criteria items have demonstrated good internal consistency (alpha=0.92), and the total diagnostic score has shown moderate correlations with measures of gambling severity (r=0.31–0.50).

National Opinion Research Center* DSM-IV *Screen for Gambling Problems (NODS). The NODS is a seventeen-question clinician-administered interview based on the *DSM-IV* diagnostic criteria. The NODS includes both a lifetime and a past-year time frame, and the past-year items are asked only if the subject endorses the corresponding lifetime items. An individual with a score of zero is considered a low-risk gambler; one with a score of one or two is an at-risk gambler; while scores of three or four identify a problem gambler; and scores of ≥5 identify a pathological gambler. In initial studies, the NODS has demonstrated test-retest coefficients of r=0.99 and r=0.98 for lifetime and past year, respectively.

Gambling Assessment Module (GAM). The GAM is a structured diagnostic gambling interview that examines eleven different types of gambling activities. The GAM can be administered by a clinician, as well as in a self-report or computerized format. The GAM has demonstrated good test-retest reliability (kappa=0.51–0.79) and poor-to-good validity on specific diagnostic criteria when compared to clinician ratings (kappa=0.0–0.7).

Gambling Behavior Interview (GBI). The Gambling Behavior Interview (GBI) is a 106-item structured interview of problem gambling behaviors used to measure *DSM-IV* diagnostic criteria for PG. The GBI has a twelve-month time frame and consists of eight content domains: (1) gambling attitudes (4 items), (2) frequency of different types of gambling (15 items), (3) time and money spent gambling (4 items), (4) gambling frequency at different venues (7 items), (5) South Oaks Gambling Screen (25 items), (6) *DSM-IV* diagnostic criteria (10 items), (7) research diagnostic items (32 items), and (8) demographics (9 items).

The ten diagnostic criteria have demonstrated high factor loadings, ranging from 0.60 to 0.87. Convergent validity ranged from r=0.32 to r=0.90 and a standard *DSM-IV* cut score of five yielded respectable overall diagnostic accuracy (0.91), with good sensitivity (0.83) and a low false negative rate (0.13).

MEASURES OF GAMBLING SEVERITY AND TREATMENT RESPONSE: SELF-REPORT MEASURES

Gambling Symptom Assessment Scale (G-SAS). The G-SAS is a twelve-item, self-rated scale assessing gambling urges, thoughts, and behaviors during the previous seven days. Each item is rated zero to four with a possible total score of forty-eight. Higher scores reflect greater severity of PG symptoms. The G-SAS has demonstrated good one-week test-retest reliability (r=0.56–0.70) and high internal consistency (alpha=0.86–0.89). In terms of validity, G-SAS scores showed excellent correlation with the PG-YBOCS in terms of change during treatment (r=0.81).

MEASURES OF GAMBLING SEVERITY AND TREATMENT RESPONSE: CLINICIAN-ADMINISTERED MEASURES

Pathological Gambling Modification: Yale-Brown Obsessive Compulsive Scale (PG-YBOCS). The PG-YBOCS is a ten-item, clinician-administered scale that rates gambling symptoms within the last seven days, on a severity scale from zero to four for each item (total scores range from zero to forty with higher scores reflecting greater illness severity). The first five items of the PG-YBOCS are the gambling urge/thought subscale (time occupied with urges/thoughts; interference and distress due to urges/thoughts; resistance against and control over urges/thoughts), and items six through ten are the gambling behavior subscale (time spent gambling and amount of gambling; interference and distress due to gambling; ability to resist and control gambling behavior).

The PG-YBOCS has demonstrated excellent inter-rater reliability (ICC=0.97), internal consistency for the total score (alpha=0.97), as well as for the urge/thought (alpha=0.94) and behavior (alpha=0.93) subscales, and excellent validity with the SOGS (r=0.89). Good sensitivity to change was shown by comparison to the Clinical Global Impression scale score (r=-0.69).

Canadian Problem Gambling Index (CPGI). The CPGI is a thirty-one-item measure with nine items scored as a measure of gambling severity. The CPGI problem gambling total score is the sum of the nine items (scored from zero "never" to three "almost always"). The interpretation of the total score ranges from zero (non-gambling) to a score of $\geq$8 (problem gambling). The CPGI has demonstrated good internal consistency (alpha=0.84) and four-week test-retest reliability (r=0.78). The CPGI scores correlate highly with those derived from the SOGS (r=0.83) and *DSM-IV* (r=0.83).

Gambling Treatment Outcome Monitoring System (GAMTOMS). The GAMTOMS is a multidimensional assessment system that includes the following instruments: (a) gambling treatment admission questionnaire, (b) primary discharge questionnaire, (c) client follow-up questionnaire, (d) staff discharge form, (e) significant other intake questionnaire, and (f) significant other follow-up questionnaire. Internal consistency for the scales has ranged from alpha=0.59 to 0.79. Validity of the gambling frequency section was modest based on correlation with the TLFB for the past four weeks (r=0.55).

Clinical Global Impressions: Pathological Gambling (CGI). The Clinical Global Impressions (CGI) is a clinician-administered instrument consisting of two reliable and valid seven-item Likert scales used to assess severity and change in clinical symptoms. The improvement scale ranges from one = "very much improved" to seven = "very much worse," whereas the CGI severity scale ranges from one = "not ill at all" to seven = "among the most extremely ill." The CGI has been used to assess PG severity and to measure "global gambling improvement" in psychopharmacological studies. CGI scores have been highly correlated with PG-YBOCS (r=0.89) and G-SAS (r=0.78–0.81) scores.

Addiction Severity Index (ASI). The Addiction Severity Index (ASI) was modified for PG to include six gambling items that are scored to create a composite score, the Gambling Severity Index (ASI-G). The ASI-G has demonstrated satisfactory reliability (alpha=0.73–0.90) and validity (r=0.57–0.75 with the SOGS).

TimeLine Follow-Back (TLFB). The TimeLine Follow-Back (TLFB) assesses the number of days and amount of money spent gambling over a six-month period. The TLFB has shown adequate three-week test-retest reliability (r=0.42–0.98) for both days and dollars gambled. Agreement with collaterals was fair to good with intra-class correlations of 0.46 to 0.65 for both days and dollars gambled. The TLFB has been adapted to assess gambling over a four-week period. The TLFB showed modest correlations with other measures of gambling frequency (r=0.24–0.53).

Multiple instruments have been developed in response to a need to detect and measure problem gambling. No single instrument is best suited for all purposes. Instead a variety of instruments are available, each with both advantages and disadvantages. In choosing an instrument to use, clinicians should consider the sample to be studied, the purpose of the assessment, the length of the battery, and the psychometric properties of the instrument.

The existing instruments all require additional psychometric evaluation, particularly with regard to specific populations. Information generated from these studies enables clinicians and researchers to make more informed decisions as to how, within specific settings and for specific purposes, to best identify, assess, and monitor individuals with gambling problems.

See also **Gambling Addiction: Epidemiology; Gambling as an Addiction.**

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GAMBLING ADDICTION: EPIDEMIOLOGY.

Gambling is a common activity in almost all societies around the world. Evidence of gambling has been found in early civilizations and throughout history. Gambling may be defined as risking something of value on the outcome of an event when the probability of winning or losing is determined by chance (Korn & Shaffer, 1999). Although the vast majority of individuals who gamble never experience any adverse consequences from the behavior, it is estimated that approximately 5 percent of adults in the United States (as many as ten million people) have serious problems related to gambling. An additional 1 percent (around two million people) of the population meet criteria for pathological gambling diagnosis. For this reason, pathological gambling is gaining increasing attention from patients, clinicians, and policy makers. It is considered to be an impulse control disorder characterized by persistent and recurrent maladaptive gambling behavior resulting in damage to vocational, employment, family, and social interests. It is also associated with financial losses and legal problems, along with medical and psychiatric comorbidity (American Psychiatric Association 2000). In 1980, the American Psychiatric Association officially included pathologic gambling in the *Diagnostic and Statistical Manual of Mental Disorders*, third edition (*DSM-III*), and it remains in the fourth edition (*DSM-IV*).

There is considerable debate about the appropriate conceptualization of pathological gambling and its place in psychiatric nosology. There are two dominant models of pathological gambling: a non-pharmacologic addiction and an obsessive-compulsive spectrum disorder. The data available from different areas seem to converge, showing that pathological gambling has characteristics that are similar to those of a substance use disorder, and less closely resemble those of obsessive-compulsive disorder, although those conceptualizations are not mutually exclusive. Pathological gambling and substance use disorders share many features: an intense desire to satisfy the need, loss of control over the behavior, periods of abstinence and tolerance, recurrent thoughts about the behavior, and continued engagement in the behavior despite negative consequences. One important difference is that substance use is generally egosyntonic (i.e., the individual does not experience his/her condition as problematic), while obsessions and compulsions are most often ego-dystonic (i.e., the individual experiences subjective distress from his/her condition).

RAPID GROWTH OF LEGALIZED GAMBLING

Historically, gambling in the United States was not considered a major recreational pastime until the largest continuous expansion ever of legalized gambling that began during the last quarter of the twentieth century. Gross gambling revenues have increased dramatically. Data suggest that the total expended on gambling, including that occurring in casinos, through lotteries, and in other settings (after accounting for winnings), was about $91 billion in 2006, up 7.7 percent from 2005, and

representing 0.7 percent of the U.S. gross domestic product (GDP). That compares with $45.1 billion expended in 1995, which represented 0.6 percent of U.S. GDP. In the 1990s, there were major increases in the availability of some forms of gambling (casino and lottery) and it was initiated in new locations (riverboats and Native American reservations), including many that were immediately accessible (convenience stores). By the end of the twentieth century, gambling in the public mind had shifted from being associated with immorality, personal deviance, and crime to become a major and socially acceptable form of entertainment. As of 2008, lottery and casino gambling are the most prominent forms of legal gambling in the United States, and there is no indication that the trend is slowing.

The factors contributing to an increase in legalized gambling include the perceived need by governments for lottery revenue to avoid raising taxes and to stimulate economic growth in distressed areas. Also contributing are the efforts of gambling entrepreneurs in the private sector and the simultaneous development of new forms of gambling technology, principally electronic gaming devices.

The private gaming industry and state governments trumpet gambling as exciting entertainment that also brings the benefits of more jobs and lower taxes. However, gambling is not solely a societal plus. When gambling is legalized and made more accessible, the number of people who engage in it increases and a certain percentage of those new gamblers develop a gambling problem. Adverse effects of pathological gambling, such as co-occurring substance use disorders and increased rates of bankruptcy, divorce, and crime have been found to be severe in clinical samples of pathological gamblers. Assessment on a large scale of these social costs has only just begun (Lesieur 1998).

PREVALENCE OF PROBLEM GAMBLING

The first national study of gambling and problem gambling in 1974 indicated that 0.8 percent of the sample had at some time in their lifetime been probable pathological gamblers, with another 2.33 percent being potential pathological gamblers (University of Michigan Survey Research Center, 1976). The second federally supported national study was conducted by the National Gambling Impact Study Commission (NGISC) in 1999. It found that 1.2 percent (2.5 million) of the adult population were considered to be probable pathological gamblers in their lifetime and 1.5 percent (three million) were lifetime problem gamblers (National Research Council, 1999). In another major national survey, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), conducted during the period 2001–2002, the prevalence of pathological gambling was 0.42 percent among the adult general population (Petry et al., 2005) with an additional 5 percent of adults being considered problem gamblers (Blanco et al., 2006).

SUBGROUPS AT RISK

An important consideration in the epidemiology of gambling is how pathological gambling affects various groups. Evidence suggests that men, youth, unmarried people, people with low income, and ethnic minorities are at increased risk of pathological gambling. The reasons for the overrepresentation in these groups are an active area of research that could help to elucidate the etiology of pathological gambling.

Gender. Prevalence rates of pathological gambling are higher in men than in women. The reasons for gender difference in prevalence rates are unknown, but are likely to be multifactorial. First, men appear to engage in regular gambling behavior more often than women. It is possible that increased exposure to gambling opportunities may partially account for prevalence differences. Social norms may oppose gambling (or higher levels of gambling) more strongly in women than men, exerting a protective effect in certain otherwise vulnerable individuals. Studies have shown different motivations to gamble in men and women, with men possibly more driven by underlying impulsivity and economic incentives, and women more motivated by emotional reasons. There are also differences in the types of gambling activities and venues among men and women with pathological gambling. Specifically, men are significantly more likely to engage in forms of gambling such as sports betting or stock trading that can be done over the phone or electronically and are therefore easily available regardless of the individual's

location. In contrast, women are more likely to engage in the types of gambling that are more often associated with escape, rather than action or strategies (Blanco et al., 2006).

Age. Gambling rates are higher among adolescents and in young adults and tend to decrease with age. However, due to the cross-sectional nature of the available data it is unknown whether differences in prevalence across age groups are due to period effects. Of concern is that there has been a substantial increase in adolescent gambling rates in the past two decades. It is estimated that 50 percent to 90 percent of adolescents gamble in a given year, despite legal restrictions on underage gambling, and 3 percent to 8 percent of adolescents are pathological gamblers.

Also of concern is that young pathological gamblers are underrepresented in treatment. Pathological gambling in adolescents has been associated with poor school or college performance, delinquency or illegal behaviors, higher rates of tobacco and alcohol use and drug abuse, risky behaviors such as having multiple sexual partners, disruption of familial relationships, low self-esteem, depressive symptoms, and suicidal ideation and attempts.

Ethnic Minorities. Several studies in the United States and other countries have suggested that some ethno-racial minorities may be at increased risk for disordered gambling. In the case of Native Americans, the establishment of casino gambling on several reservations through the 1988 Federal Indian Gaming Regulatory Act may have increased exposure to gambling activities in this population, leading to an increased risk for disordered gambling among vulnerable individuals. Increased risk for problem and pathological gambling in certain ethno-racial groups is partially due to the highest prevalence of risk factors in those groups. For example, Native Americans have been consistently found to have a higher prevalence of psychiatric disorders, specifically alcohol and drug use disorders, than any other ethno-racial group, a factor strongly associated with problem and pathological gambling. Cultural factors also appear to influence the prevalence of problem and pathological gambling in ethnic minorities. For example, gambling is part of the tradition, history, and lifestyle of some Asian cultures. In other cultures, acceptance of magical thinking and the existence of fate may allow such beliefs to be extended to gambling. Difficulties related to post-immigration adjustment, such as unemployment, language barriers, and social isolation, which can affect many members of ethno-racial minorities, have been also associated with problem and pathological gambling among Asians.

Socioeconomic Factors. Lower socio-economic status is consistently associated with increased pathological gambling rates. One hypothesis concerning the basis for this relationship is that individuals with less education are less able to understand the probabilities associated with gambling, but little empirical evidence is yet available to support this. Other researchers have suggested that this relationship could be explained by the poorer economic conditions experienced by some people, resulting in a strong motivation to engage in gambling behaviors in order to increase income.

Marital Status. Pathological gamblers are more likely to be divorced or separated. It has been suggested that separation and divorce are a result, rather than a cause for the development of pathological gambling. Others have suggested that pathological gamblers may be less likely to get or stay married because of an inability to maintain stable relationships.

PREDISPOSING FACTORS

Personality traits such as high impulsivity and extraversion have been associated with problem gambling. Problem gambling often occurs jointly with substance abuse, mood disorders, and personality disorders. In certain cases, gambling may serve to provide escape from depression or anxiety. Offspring of pathological gamblers are at increased risk of pathological gambling, because they are exposed to parental approval of gambling, though genetic factors also play a role. Earlier onset of gambling behavior seems to be directly related to a greater likelihood of progression to pathological gambling.

Community-level Factors. The prevalence of gambling problems is affected by many factors, including the number of legal and accessible gambling opportunities, as well as illegal ones. Prevalence rates may also be affected by the increasing

availability of forms of electronic gaming (slots, video poker, video lottery terminals). This form of gambling involves an interaction between person and machine, which provides the opportunity for more frequent play and reinforcement than other forms of gambling. Because of the short time between the bet and the outcome, this form of gambling is likely to become more addictive. In addition, electronic gaming is often available twenty-four hours a day, which further increases its addictive potential.

Higher prevalence rates for problem gambling may also result when there is an increased societal acceptance of financial risk-taking. Although many forms of financial risk-taking, such as investing in stocks and other financial markets, are socially acceptable, they can also become arenas for problem and pathological gambling. In 1997 the U.S. Securities and Exchange Commission acknowledged for the first time that problem gambling occurs in the financial markets, distributing a pamphlet on investor problem gambling (Connecticut Council on Problem Gambling, 1997). The presence of the Internet has also increased the accessibility of gambling opportunities. As a result, the number of gambling sites available and the number of online gamblers have been increasing rapidly, as indicated by the sharp increase in Internet gambling revenues, from $445.4 million in 1997 (Barry, 1998) to $5.9 billion in 2005, according to Christiansen Capital Advisors (CCA 2007). As a response to this, in 2006, Sen. John Kyl (R-Ariz.) and Senate Majority Leader Bill Frist (R-Tenn.) secured the passage of the first federal legislation restricting the rapidly increasing online gambling industry when they attached the Unlawful Internet Gambling Enforcement Act (UIGEA) to federal legislation crafted to increase the security of U.S. ports.

TREATMENT INTERVENTIONS

Despite increasing awareness of the disorder, most pathological gamblers do not seek treatment. If they do, they may first seek treatment for a comorbid disorder rather than for the pathological gambling itself. Pathological gambling remains largely undiagnosed and untreated, even among high-risk populations such as youth and substance abusers. The treatment of pathological gambling is complicated by high rates of comorbidity with mood, substance use, and personality disorders (Petry et al., 2005) and high rates of treatment dropout. Treatment compliance is of great concern when it comes to pathological gambling as it is for other addictions. Promising evidence suggests that pathological gambling can be treated successfully with pharmacotherapy and psychotherapy.

Pharmacotherapy. Although several medications have been examined as potential treatments for pathological gambling, there are no medications approved by the Food and Drug Administration for its treatment. Selective serotonin reuptake inhibitors (SSRIs) have shown mixed results. Some reports have shown beneficial effects of fluvoxamine (Hollander et al., 2000) especially in young men (Blanco et al., 2002). A single-site, double-blind, randomized clinical trial of paroxetine showed that gambling behavior decreased after sixteen weeks of treatment, but in a later study it failed to show efficacy compared with placebo. A study of sertraline (Saiz-Ruiz et al., 2005) further supports the finding that antidepressant medication may be beneficial only for some pathological gamblers. In studies in which participants had few or no signs of comorbid anxiety or depression, treatment with SSRIs were effective in reducing gambling behaviors.

Other researchers have tested the use of opioid antagonists in the treatment of pathological gambling, with promising results. A study using naltrexone in pathological gamblers showed high rates of response (Kim, 2001). This medication was more effective in gamblers with more severe urges to gamble. Also, in a clinical trial, nalmefene was superior compared with placebo in reducing gambling urges and behavior (Grant et al., 2006), although the study had very high dropout rates. Overall, although several medications have shown promise, further research is needed into this area.

Psychotherapy. Although a vast number of theoretical approaches to treat pathological gamblers exist, limitations on patients' follow-up and the inappropriate use of treatment outcomes makes it difficult to evaluate the efficacy of these approaches. However, several controlled studies on the efficacy of cognitive-behavioral therapy for patients with

pathological gambling have yielded promising results (Sylvain et al., 1997; Echeburua et al., 1996; Petry, 2005). According to a cognitive-behavioral model, stimuli that become associated with gambling can over time develop into triggers for gambling. Once a trigger is encountered, it leads to an involuntary response of heightened autonomic arousal that is accompanied by gambling-related cognitions (e.g., "This is my lucky day") and urges to gamble. Whether or not a person gambles is mediated by coping skills. Treatment involves interventions that aim to enhance coping skills such as stimulus control and response prevention, problem-solving skills, assertiveness training, erroneous cognition modification, relaxation training, and relapse prevention (Petry, 2005).

Step-based Program. The most common step-based program for problem gamblers over the world is Gamblers Anonymous. This program uses a twelve-step program adapted from Alcoholics Anonymous and offers peer support for its attendants. This program is recommended as a complement to professional treatment, but seems to have very limited effect when used as the only intervention (Petry et al., 2006).

GROWTH OF COUNCILS ON PROBLEM GAMBLING

To meet the challenges of problem gambling, which increased with the growth of gambling in the last quarter of the twentieth century, councils on problem gambling have been created in the United States and Canada. As spiritual advisor to Gamblers Anonymous, Monsignor Joseph Dunne, along with recovering compulsive gamblers and family members, founded the National Council on Problem Gambling (NCPG) in 1972. The first state affiliate of the NCPG was Connecticut in 1980, and by 2000 there were thirty-four state affiliate councils. The NCPG was the first professional organization to educate the public about compulsive gambling as a serious public health problem and to advocate for treatment services. Other major priorities of the NCPG and its affiliates include sponsoring helplines, conducting prevention programs, training human services personnel, conducting surveys on problem gambling, and collaborating with a variety of relevant organizations, including the public and private gaming industry.

RECOMMENDATIONS OF THE NATIONAL GAMBLING IMPACT STUDY COMMISSION (NGISC)

The 1999 examination by the NGISC was the most extensive and systematic study of gambling in the United States. The study made seventy-four recommendations for changes in policies and practices for the public, private, and Native American sectors of the gambling industry, including state regulators and the federal government. As of 2008, most of these recommendations have not been implemented, which suggests that this is an important area for future advocacy.

Some of the major recommendations include:

- A pause in the processing of all new gambling premises licenses applications to allow for adequate assessment of the gambling establishments already in place
- A rollback of all convenience gambling in communities and a halt to authorization of all new convenience gambling
- A restriction of the minimum legal gambling age to twenty-one
- A ban on betting on collegiate and amateur athletics
- A ban on all aggressive gambling advertisements and the creation of responsible gambling advertisement guidelines
- Prohibition of Internet gambling not already authorized
- A ban on ATM and credit card machines within or near the immediate gambling area
- Gambling establishment policies to ensure the safety of children and prevent underage gambling
- School programs from the elementary through college level should include warning of the dangers of gambling

See also **Gambling as an Addiction.**

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GAMMA-AMINOBUTYRIC ACID (GABA). Gamma-aminobutyric acid (GABA) is an amino acid neurotransmitter that is derived from glutamate by a single-step decarboxylation (a chemical reaction in which a carboxyl group [-COOH] is split off as carbon dioxide). GABA is the most abundant (in micromolar concentrations/mg of protein) inhibitory neurotransmitter, and it is found throughout the animal kingdom. Its role as a neurotransmitter was first defined for the inhibitory nerve in lobster muscle, where GABA accounted for the total inhibitory potency of nerve extracts. A central inhibitory neurotransmitter role for GABA was securely established only when selective antagonists (such as bicuculline) discriminated GABA receptors and pathways from those involving glycine, a related inhibitory amino acid neurotransmitter.

GABA actions, and receptors for GABA, have been linked to central nervous system sedatives such as alcohol and benzodiazepines. Recently, the GABA system has been targeted for the treatment of substance abuse. Vigabatrin is an irreversible inhibitor of GABA-transaminase, an enzyme that breaks down GABA, thereby increasing intracellular GABA concentrations. The drug effectively inhibits increases in brain dopamine concentrations induced by cocaine, amphetamine or methamphetamine, alcohol, nicotine, phencyclidine, heroin, or morphine. Further, increased GABA tone blocks behaviors associated with drugs of abuse, including drug self-administration, conditioned place preference, and the reinstatement of both of these phenomena. Clinical trials using the anticonvulsant vigabatrin in cocaine-

dependent subjects have yielded promising results. In addition, studies have demonstrated that targeting the GABA system may also be an effective strategy for treating binge-eating disorder.

See also **Dopamine; Glutamate; Neurotransmitters.**

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GANGS AND DRUGS. The gang is an American phenomenon. Reports of groups of youth involved in criminal activities called "gangs" emerged over 200 years ago in the United States (Fagan, 2001). Since then, the gang has held a particular fascination in the United States, and young people in gangs are the contemporary image of the rogue, the bad guy, the criminal "other" (cf. Jefferson, 1993; Sanders, 2005). In the twenty-first century, gangs remain an important criminal justice concern, as they are responsible for a disproportionate amount of crime. For instance, in large cities such as Los Angeles and Chicago, half of the total number of homicides has been considered "gang related" (Egley & Ritz, 2006). As of 2004, statistics indicate that approximately three-quarters of a million gang members were active in the United States (Egley & Ritz, 2006). These numbers are based largely on police records, and more gang youth may exist due to their hidden nature (Valdez & Kaplan, 1999).

While ganging has traditionally been a male phenomenon, research indicates the number of female gang members has risen significantly in recent years (Miller, 2001a; Miller, 2001b). Esbensen and Lynsky (2001, p. 98), for instance, reported in their findings that "there are more girls in gangs than is commonly assumed" whereby 38 percent of all gang members in their 8th grade sample were females. Young women in gangs are no longer considered strictly to be sexual auxiliaries of male gangs, but are rather autonomous groups who engage in crime and violence at levels paralleling their male counterparts (Miller, 2001b; Moore & Hagedorn, 2001; however, see Wang, 2000).

Defining what exactly constitutes a gang has been an important focus of gang research, and the definition has changed over the years (Brotherton & Barrios, 2004; Klein, 1971, 2006; Miller, 1958; Sanders, 1994; Spergel, 1964, 1995; Yablonsky, 1962). One contemporary definition is offered by Klein, who classifies a gang as "any durable, street-oriented youth group whose own identity includes involvement in illegal activities" (Klein, 2006). This definition is similar to the one utilized by law enforcement in some states such as California (see California Penal Code 186.22 [f]). Gangs can be further broken down by type based on their structure and activities. The Klein/Maxson gang typology indicates characteristics of five different gang types (Klein & Maxson, 2006):

1. The traditional gang: Such gangs are well-established (over 20 years old) and regenerate themselves through the recruitment of younger members. They often have cliques separated by age, location of neighborhood or gang status, with a wide age-range of members (e.g., 10–30 years old). Such gangs are very large, numbering in the hundreds, and they strongly identify with a particular neighborhood or "turf."
2. The neo-traditional gang: Similar to the traditional gang, but somewhat smaller (e.g., 50–100 members, though it can reach a couple of hundred) with a shorter length of existence (e.g., 10 years or less).
3. The compressed gang: Unlike the above gangs, the compressed gang is small (50 members or less), has no subgroups, and a narrow age range (i.e., 10 or fewer years between younger and older members). These gangs have been around less than 10 years and may be territorial.
4. The collective gang: Unlike the compressed gang, the collective gang has a wider age range (i.e., 10 or more years between younger and older members), a larger size (around 100 or more members), and has been in existence longer (i.e., 10–15 years). No subgroups exist in this gang. The collective gang may be territorial.
5. The specialty gang: Whereas the previous gangs engage in a wide variety of offenses, those in the specialty gang engage in particular offenses (e.g.,

drug selling) for which they become known. Issues of territoriality are related to these offenses. Such gangs are usually small, with 50 members or less, and likely have been around less than 10 years.

Another gang type could be added to this typology: the multinational gang. One gang in particular, Mara Salvatrucha 13—commonly known as MS-13—may be considered a multinational gang. Little academic research on MS-13 has emerged, and most of what is known about the gang is drawn from media reports or intelligence assessments (Darnton, 2005; Del Barco, 2005; Federal Bureau of Investigation, 2008; National Drug Intelligence Center, 2002). Based on these data, it can be gathered that MS-13 consists of Latinos from Honduras, Guatemala, and, in particular, El Salvador. MS-13 cliques can be found throughout several nations including the United States, Canada, and some European countries. Moreover, MS-13 has reportedly been involved in crimes typical of organized syndicates, such as weapons and drug smuggling, but also human trafficking, which is an offense unique to this type of gang.

Debates continue on whether gang characteristics are clearly outlined or vague, antisocial or constructive, or responsible for a large portion of crime and violence or a fraction of it (see Brotherton & Barrios, 2004; Egley & Major, 2004; Katz, 2000; Katz & Jackson-Jacobs, 2004; Klein, 1971, 2006; Miller, 2001a; Sanders, 1994; Spergel, 1995, cf. Sanders & Lankenau, 2006). Outlining what exactly constitutes a gang and the different types of gangs is relevant for a discussion on drug use and sales, because most gangs *do not* sell drugs and some gang members have very hostile attitudes toward the use of certain drugs.

GANG YOUTH AND SUBSTANCE USE

According to national sentinel data, such as Monitoring the Future, the National Survey on Drug Use and Health, and the Youth Risk Behavior Survey, cannabis and alcohol are the most commonly reported substances used by young people in the United States (Eaton et al., 2006; Johnston et al., 2008; Substance Abuse and Mental Health Services Administration, 2007). Correspondingly, the use of these drugs is the most commonly reported among gang youth (Fagan, 2001).

Studies specifically on gangs have indicated that at least 90 percent of their samples have ever used alcohol, and between 80 percent and 90 percent have ever used cannabis (e.g., Hagedorn, 1998; Mata et al., 2002). Much of gang life consists of "hanging around"—a relatively consistent finding among gang researchers over time (Klein, 1995; Sanders, 1994; Short & Strodbeck, 1965; Vigil, 1988). During such times, the use of alcohol and cannabis is a prominent activity. Hunt and Joe-Laidler (2001) discuss various symbolic roles of alcohol in the lives of gang members related to issues of displaying masculinity, maintaining a "cool" image, facilitating violence, gang initiation, and ritualistic mourning (e.g., pouring alcohol on the ground in remembrance of deceased peers; see also Moore, 1991; Valdez et al., 2006; Vigil, 1988). Similar to much research on gang males, Joe-Laidler and Hunt (1997) also reported that among both African American and Latino gang females, "hanging out" and "partying" were major activities, where drinking alcohol and smoking cannabis featured prominently (see also Harris, 1988).

Gang members also use a variety of other drugs. Phencyclidine (PCP) and crack cocaine have been found among Latino gang youth in East Los Angeles (Moore, 1991; Vigil, 1988; see also Joe-Laidler and Hunt, 1997). Valdez et al. (2006), in their study of gang members, found approximately 90 percent of their sample had ever used cocaine, 57 percent had ever injected heroin, 35 percent had ever used inhalants, and 29 percent had ever used amphetamines. Robinson (2001) noted that up to 50 percent of gang members reported ever using crystal methamphetamine, a drug commonly associated with Caucasians and outlaw motorcycle groups. Brotherton (1996) also reported on a wide variety of substance use among gang females in San Francisco including crack, PCP, and LSD (i.e., acid). Hagedorn and Devitt (1999) reported that daily cocaine use was prevalent among the Latina gang members, with two-thirds indicating such behavior, while only around a quarter (27.8%) of the African American gang females used cocaine daily. However, about twice as many African American gang females than Latina gang members in Hagedorn and Devitt's study reported going to school "while high" (presumably on cannabis) on a daily basis.

Some gang researchers have indicated that gang members have harsh views of some hard drugs. Vigil (1988), for instance, reported that Latino gang members had very critical attitudes towards heroin use, and similar sentiments were expressed by Latino gang members in South Texas (Valdez & Sifaneck, 2004). Likewise, Chin (1996) found that while Chinese gang members used alcohol, few were regular users of cannabis and very small percentages used "hard" drugs such as cocaine or heroin.

Emerging topics of concern related to substance use, such as non-medical prescription drug use and polydrug use (i.e., the simultaneous or sequential use of two or more substances), have received peripheral attention in the research literature on gang youth. Sanders et al. (2007) found that many gang youth reported lifetime rates of using prescription drugs, particularly opiates (e.g., Vicodin) and benzodiazepines (e.g., Valium; see also Valdez et al., 2006). Moreover, many of the gang youth in the Sanders et al. study reported polydrug use, particularly the use of alcohol alongside cannabis, but also alcohol, cannabis, and one other drug, especially crystal methamphetamine, powder cocaine or crack cocaine (cf. Bennett & Holloway, 2005). Cannabis joints containing crack cocaine were also reported by Sanders et al. (cf. Bourgois, 1995). Valdez et al. (2006) reported that 44 percent of their sample had ever used a mixture of heroin and cocaine (i.e., "speedballs").

Gang members clearly use a variety of substances. Comparative research often indicates that gang youth use *more* drugs and alcohol in comparison to their non-gang peers. Evidence from several longitudinal studies on youth development in North America (Denver, Rochester, Seattle, Pittsburgh, and Montreal) all indicate that gang youth, compared to non-gang youth**,** not only have higher rates of crime and violence perpetration, but also drug and alcohol use (see, e.g., Thornberry et al., 2003).

In Seattle, Hill and colleagues (2001) found that gang youth were more likely to binge drink alcohol and use marijuana in comparison to non-gang youth. Over half of the gang youth in the Hill et al. study had used marijuana, though only about a quarter of non-gang youth had done so. In Rochester, Thornberry et al. (1993) found that gang youth reported drug use that was four to five times higher in comparison to the non-gang youth in the sample. In Montreal, Gatti et al. (2005) found that rates of drug use for gang youth were three to four times higher when compared to non-gang youth. In a similar vein, Bjerregaard and Smith (1993), utilizing the Rochester data set, found that gang females were more likely to report alcohol and marijuana use in comparison to the non-gang females. Moreover, gang females have been found to report higher involvement in drug sales and drug use than the non-gang males (Esbensen & Winfree, 1998).

Even studies on other groups of high risk youth, such as homeless youth, find that former and current gang involvement is related to increased substance use. For instance, in a study among homeless youth in Midwestern states, Yoder et al. (2003) found that those who also identified as gang members or as gang "involved" reported higher overall rates of substance use compared to the homeless youth with no such identification. Similar findings were reported in a study by Harper and colleagues (2008) in Chicago, who found that homeless youth with gang ties were more likely to use substances (Harper et al., 2008). Further still, Harper et al. developed a "level of gang involvement scale," and found a significant positive relationship between level of gang involvement and lifetime use of alcohol and cannabis. This finding corroborates Klein's earlier work on differences he found between "core" and "fringe" gang members, with the former more likely to report greater substance use (see Klein & Maxson, 2006). Together, the comparative studies indicate the significant effect of both gang participation itself and the *intensity* of gang participation on increased levels of reported substance use (see also Walker-Barnes & Mason, 2004; Zhang et al., 1999).

Gang youth are an important criminal justice concern due to the elevated rates of crime and violence committed by gang members. Gang youth may also be considered a public health concern, as their elevated rates of substance use suggest they are at an increased likelihood of suffering from the many related negative health outcomes such as cognitive impairment, overdose, addiction, exposure to hepatitis C and HIV, and even death (Sanders & Lankenau, 2006).

GANG YOUTH AND DRUG SELLING

Media representations and law enforcement proclamations closely link drug selling with gang membership

(Curtis, 2003). It has been argued, however, that most gangs have been poorly organized to sustain a system of drug distribution (Decker, 2001; Esbensen et al., 2002; Klein, 1995; Spergel, 1995). Curtis (2003, p. 42) found that, between 1990 and 2000, drug distribution among gang youth was "inconsequential" to the overall drug market in New York City. Certain members within gangs may sell drugs but drug distribution is often reported as not being central to the gang's overall purpose (see Decker & Van Winkle, 1996). Such findings stand in sharp contrast to what is generally perceived about gang members and drug selling.

Of all the gang types discussed earlier, the "specialty" gang may be organized explicitly around drug selling. Several studies have emerged that have examined gangs that may be considered specialty gangs, particularly those involved in corporation-style crack cocaine distribution, whereby members view such distribution as "employment" or "enterprise" (Hagedorn, 1988; Padilla, 1992; Taylor, 1989; see also Decker, 2001). Drug selling in such cases is a business akin to those within the service industry such as fast food restaurants (Anderson, 1990; Ruggiero & South, 1995; Sanders, 2005). Even the language of drug selling in such instances mirrors fast food language, where users are talked about as "customers" and selling drugs to them is discussed as "serving" (Padilla, 1992; Ruggiero & South, 1995; Sanders, 2005; Williams, 1989).

Moore and Hagedorn (2001) reported that selling drugs is among the most common offenses committed by female gang members. Miller and Decker (2001) indicate that approximately two-thirds (63%) of the gang females had sold marijuana and/or crack cocaine, and that approximately a quarter (22%) had sold other drugs. Joe-Laidler and Hunt (1997) found that, among African American gang females, selling crack was a primary source of income, and that among Latina gang members, over one-third sold drugs, primarily cannabis and cocaine. Hagedorn and Devitt (1999) found that among African American females, those who sold drugs on their own were equal in proportion to those who sold drugs as part of "the guy's operation" (each at 8.3% of the sample). In contrast, very few (1.9%) of the Latina gang members sold drugs on their own but more than two-fifths (42.3%) sold drugs alongside the gang males. Taylor (1993) notes that African American female gang members were directly involved in crack cocaine distribution.

The phrase "don't get high on your own supply" is a colloquialism cautioning individuals tempted to use the drugs they sell (Sanders, 2005). While selling crack cocaine may be sanctioned among fellow gang members, using the drug may not be. Taylor (1989) and Fagan (1996), in writing about gangs who sell crack, have mentioned harsh consequences for gang members found to use the drug (Bourgois, 1995; Jacobs, 1999; Sanders, 2005). In other words, selling crack was not viewed as problematic among gang youth, but using the drug was a completely different story.

Valdez and Sifaneck (2004) offer a valuable portrait of the relationship between drug users and drug sellers within Mexican American gangs in South Texas. Similar to other researchers (e.g., Klein, 1995), Valdez and Sifaneck identified two different gang types: the street gang and the drug gang. In the street gang, the authors identify two types of drug sellers: the homeboy and the hustler. The homeboy is a drug user/seller who sells a small amount of drugs in order to cover the costs of personal use and perhaps generate a small income. The hustler, in contrast, sells drugs strictly for personal profit (see also Decker, 2001). While the drug profits the hustler, the earnings do not support the street gang; the hustler benefits from the protection the gang offers as part of membership. The drug gang also has two types of drug sellers: the slanger and the baller. The slanger, like the homeboy, is a drug user/seller, who sells small portions of drugs to offset the costs associated with personal use and earn a small profit. The baller, in contrast, controls drug distribution business in a gang that is organized around such an endeavor, whereby profits from this business benefit the entire gang. Ballers may also be users but are less ubiquitous and rarely seen.

Most youth in gangs, like most young offenders, do not specialize in one type of offense, but engage in a variety of offenses (Decker, 2001; Klein, 1995). And while gang members may sell drugs, and their gang may offer some sort of direct or indirect support for drug distribution, most gangs do not focus on selling drugs and are not organized to do so.

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BILL SANDERS

GANJA. Ganja is a Hindi word (derived from Sanskritic) for the hemp plant, *Cannabis sativa* (marijuana); the term *ganja* entered English in the late seventeenth century. Ganja is a selected and potent preparation of marijuana used for smoking.

The hemp plant was introduced into the British West Indies by indentured laborers from India who arrived in Jamaica in 1845. Considered to be a "holy" plant, ganja is often used in religious ceremonies in both countries. The Indian Hemp Drug Commission traced the origin of ganja use to India.

Although usually smoked, *Cannabis* may also be mixed with foods or drinks; it is considered a remedy for many ailments in herbal medicine. A medical-anthropological study of ganja users in Jamaica was conducted in 1972; the results revealed little evidence of a deleterious effect among users, as compared with nonusers. These conclusions were criticized, however, by investigators who claim that the tests of maturation and mental capacity that were used were not sensitive enough to detect decrements in higher level mental skills or motivation.

See also **Bhang; Plants, Drugs From.**

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LEO E. HOLLISTER

GENDER AND COMPLICATIONS OF SUBSTANCE ABUSE. Despite a lower overall level of alcohol and drug consumption and rates of substance use disorder, women suffer more negative physical and psychiatric consequences from substance use than men. In this entry, the evidence for gender differences in the complications of substance abuse will be reviewed in three overall areas: (1) alcohol, (2) nicotine, and (3) illicit drugs.

ALCOHOL

Gender differences in the consequences of alcohol use and abuse are extensively researched and well documented in both human populations and animal models. Women exhibit higher blood alcohol levels than men at the same level of consumption, due to smaller average body size (Lieber, 1997), body water content (Lieber, 1997), and lower gastric alcohol dehydrogenase (an enzyme that is involved in the oxidation of alcohol through the liver) activity among younger adults. Further, alcohol-dependent women exhibit higher rates of physical illness compared to alcohol dependent men including overall mortality (Klatsky, Armstrong, & Friedman, 1992), cirrhosis of the liver (Deal & Gavaler, 1994), heart attacks (Hanna, Chou, & Grant, 1997), and brain damage (Schweinsburg et al., 2003; Hommer et al., 2001). Heavy alcohol use is also a risk factor for breast cancer (Key et al., 2006). Alcohol disorders often co-occur with other psychiatric disorders such as depression and anxiety disorders. Studies suggest that women are more likely to exhibit anxiety disorders when presenting for alcohol treatment (Brady et al., 1993), but larger population-based studies have found little evidence for gender differences in rates of coexisting diseases among alcoholics (Regier et al., 1990; Kessler et al., 1996).

The consequences of heavy alcohol use during pregnancy are also well documented. In addition to Fetal Alcohol Syndrome in the offspring, even moderate use of alcohol during pregnancy is associated with adverse outcomes in the offspring. These include low birth weight and premature birth (Sokol, Delaney-Black, & Nordstrom, 2003) as well as impairments throughout childhood, including slow growth as measured up to age six and learning disorders as measured up to age 10 (Jacobson & Jacobson, 2000). Moderate alcohol use is also associated with increased risk of miscarriage and stillbirth (Kesmodel et al., 2002). Although the amount of alcohol that adversely affects the fetus is still debated, most women are advised to abstain from alcohol throughout pregnancy (Coles et al., 2000).

NICOTINE

Gender differences in the adverse effects of nicotine, particularly via cigarette use, have been consistently observed. Although it is generally believed that the acute effects of nicotine are similar in men and women, women are less likely than men to experience positive effects from nicotine. Instead, women respond to smoke stimuli, secondary social reinforcement, and other sensory aspects of the smoking experience. Clinical evidence suggests that women experience more severe nicotine withdrawal syndromes, which may contribute to a lower abstinence rate compared to men (Leventhal et al., 2007). Further, women experience greater depressive and anxiety symptoms when they stop smoking (Borelli et al., 2001) and are subject to effects involving the menstrual cycle in which stimulation and withdrawal from nicotine is stronger in the menstrual phase that immediately precedes menstruation (Mello, Mendelson, & Palmieri, 1987; Craig, Parrott, & Coomber, 1992). Despite fewer reinforcing effects of nicotine, nicotine-dependent women may be at higher risk for smoking-related diseases such as lung cancer (Zang & Wynder, 1996) as well as heart attacks than men (Prescott et al., 1998). Women also suffer reproductively from nicotine dependence, as smoking during pregnancy has been known for decades to have adverse effects on the fetus (Wilcox, 1993).

Studies show that women in smoking cessation treatment have lower rates of abstinence than men whether the treatment includes counseling, nicotine replacement therapy vs. placebo (Cepeda-Benito, Reynoso, & Erath, 2004), or a medication such as buproprion vs. placebo (Sharf & Shiffman, 2004). Some researchers hypothesize that women may have more difficulty quitting smoking due to a more severe withdrawal syndrome, greater psychiatric symptoms, or social factors, such as fear of weight gain (Borelli et al., 2001; Etter, Prokhorov, & Perneger, 2002). The development of smoking prevention and cessation treatments targeted

toward women remains a vitally important research topic, especially as evidence indicates that adolescent girls are smoking at a higher rate than boys (Johnston et al., 2007).

ILLICIT DRUGS

Gender differences in the consequences of illicit drug use are less studied, although extensive work has been done on sex differences in cocaine and stimulant addiction in animal models. These models indicate that sex differences occur at many stages of the cocaine addiction process, including more rapid acquisition of cocaine and opiates among females, more bingeing and craving during the maintenance phase, and greater risk for relapse (Becker & Hu, 2008; Lynch, Roth, & Carroll, 2002; Lynch, 2006). Further, female rats have an exaggerated behavior response as well as higher stress levels (as measured by corticosterone release) after both acute and chronic cocaine administration (Festa et al., 2003; Hu & Becker, 2003; Hu, Robinson, & Becker, 2006). These animal studies indicate a biological basis for addiction through a combination of factors including sex differences in neurotransmission and pharmacokinetics (i.e., how the body handles the drug) (Lynch, Roth, & Carroll, 2002; Becker, 1999; Carroll et al., 2004). Additionally, extensive literature shows the effect of hormones such as estrogen and progesterone in modulating the brain activity important during cocaine use and affecting toxicity of cocaine differently in males and females (Becker & Hu, 2008). Evidence from animal models also indicates that chronic cocaine administration can lead to menstrual cycle disruptions and amenorrhea (loss of menses) in females (Mello et al., 1997). The translation of this research to human populations remains an important yet complex task for addiction researchers.

Serious social consequences also adversely affect female drug users. Among illicit drug users, women experience a higher risk of physical and sexual assault (Silverman et al., 2001), although men experience more legal problems associated with drug use than women (Su et al., 1997). Infections with the hepatitis C virus and HIV are also serious health consequences of drug use, and more than half of AIDS cases in women in the United States are related to injection drug use either through personal use or sex with an injection drug user, compared with 31 percent of cases among men (Schneider et al., 2006). Interestingly, in contrast to other substances in which women have greater health risks following prolonged use, men may be at greater risk for ischemic stroke from chronic cocaine abuse, although there is some evidence to refute this (Petitti et al., 1998).

In conclusion, the harmful long-term effects of alcohol, nicotine, and illicit drugs are different between men and women. Typically, women exhibit more harmful effects of substance use disorders, including increased disease and death. More research into the consequences of illicit drug use in human populations is necessary, but animal models show robust sex differences in every phase of drug self-administration, suggesting that biological factors may affect the consequences of drug use. Regardless, research indicates the necessity of prevention and treatment efforts specifically addressing the needs of substance-using women.

See also **Fetal Alcohol Syndrome; Pregnancy and Drug Dependence; Women and Substance Abuse.**

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GENE. A gene is a unit of heredity that confers some trait or function on the organism. Most genes are thought to be essential to development and normal functioning. Genes are often a primary determinant of interpersonal differences; for example, they determine whether you have blue or brown eyes. A disrupted or mutated gene can cause serious, even fatal problems. Genes are composed of DNA and found in the chromosomes in the nucleus of a cell. At present, we are on the verge of identifying all the human genes due to the efforts of the genome projects.

See also **Chromosome.**

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MICHAEL J. KUHAR

GENE REGULATION: DRUGS. A gene, made of DNA, is transcribed to produce a messenger RNA (mRNA), which is then translated to produce a protein product. *Gene regulation* refers to alterations in the production of mRNA from a gene.

All cells of an organism contain the same genes, but not every gene is turned on (producing its mRNA) at all times. During development, different cell types and organs are generated by the selective expression of genes. Likewise, during adulthood, altered expression of genes within mature neurons mediates their ability to adapt to the environment. Such gene regulation is thought to play a crucial role in mediating positive adaptations (e.g., learning, therapeutic response to an antidepressant medication, or psychotherapy), as well as maladaptations associated with disease states (e.g., pathological responses to drugs of abuse or stress).

Gene regulation in neurons is governed by highly complex processes. DNA exists in the neuron's nucleus within chromatin, where the DNA is wrapped around complexes of histone proteins; these DNA-histone units are called nucleosomes. Genes present within tightly packed nucleosomes are inactive because they are inaccessible to the enzymatic machinery required for mRNA transcription. In contrast, genes become active when the nucleosomes become less tightly packed. This occurs when specialized proteins, called transcription factors, bind to specific sequences of DNA present within the regulatory (promoter) regions of genes. Transcription factors recruit enzymes to the genes which modify the nearby histones (e.g., by acetylation), which causes further loosening of the nucleosomes. Genes are then inactivated when other enzymes remove the acetyl groups from the histones, allowing restoration of more tightly packed nucleosomes. Transcription factors can cause the opposite effects when they bind to other responsive

genes and inhibit gene function by reducing histone acetylation and tightening nucleosomes.

This highly simplified summary of gene regulation provides a context within which individuals can begin to appreciate how a drug of abuse alters gene regulation in the brain. After a drug is taken, it enters the brain where it interacts with its initial protein target (e.g., the dopamine transporter for cocaine or mu opioid receptor for opiates); binding to the target alters the activity of endogenous neurotransmitter systems (dopamine or opioids), which alters the activity of postreceptor signaling proteins. These proteins signal to the neuron's nucleus where they alter the activity and levels of particular transcription factors. The transcription factors then bind to the promoters of certain genes, which increases or decreases the rate at which the genes produce their mRNAs, which ultimately changes the levels of protein products in the neurons. In this manner, drugs of abuse change the biochemical composition of individual neurons in the brain and cause profound changes in brain function that underlie key aspects of drug addiction.

An example of this process is the transcription factor, ΔFosB. Administration of virtually any type of drug of abuse causes the induction of a small amount of ΔFosB in important brain reward regions. Unlike most proteins, ΔFosB is highly stable, which means that repeated administration of the drug leads to the gradual accumulation of ΔFosB. As ΔFosB accumulates within the neurons, it binds to an increasing number of gene promoters where it can either increase or decrease transcription of those genes' mRNAs. Increasing evidence indicates that such ΔFosB-mediated gene regulation creates a state of heightened reward, which promotes further drug use. This research raises the interesting possibility that medications that block ΔFosB may be useful in the treatment of addiction. To determine if this is, in fact, true will require much further research. Nevertheless, studies of gene regulation offer novel insight into the molecular basis of addictive states and the hope that such knowledge will be mined one day to develop more effective treatments and possibly even cures for drug addiction.

See also **Neurotransmitters.**

ERIC J. NESTLER

GENOME PROJECT. The Human Genome Project started in 1990 with the goal of sequencing the entire human genome and the genomes of five model organisms: bacterium (*Escherichia coli)*, yeast *(Saccharomyces cerevisiae)*, nematode *(Caenorhabditis elegans)*, fruit fly *(Drosophila melanogaster)*, and mouse *(Mus musculus)*. The human genome is the complete set of deoxyribonucleic acid (DNA, the genetic material) in a typical human cell; it is approximately three billion nucleotides, contained in 22 pairs of autosomal chromosomes, two sex chromosomes (X and Y), and the mitochondrion. The human genome contains all of the genetic information needed for the development of a human from a single cell. The human genome is diploid, meaning there are two copies of each chromosome, which are nearly, but not completely, the same. The original target for the Human Genome Project was to get a reference sequence that would represent a haploid copy (equivalent to one copy of each chromosome).

The Human Genome Project, by generating the genome sequence and knowledge of genetic variations and stimulating development of technologies that allow one to measure the variations present in an individual, has greatly stimulated research to find which genes contain variations that can affect the risk for contracting complex diseases such as alcoholism and other addictions, diabetes, and various cancers. Continuing work on annotating the genome (i.e., determining which sequences encode genes or other functional elements) and understanding the functions of many sequences is necessary; it will further aid in finding and understanding how genetic variations affect these diseases.

The Human Genome Project was an international effort that drove advances in DNA sequencing technology and the computational tools to analyze the vast amounts of data generated. Projects to explore how the genetic information might have an impact on individuals and society were also part of the effort. The initial goals of creating genetic and physical maps of the genome were completed early in the process and contributed to the ability to map genes whose variations affect the risk for diseases. The public genome project adopted a strategy based on mapping the genome, creating a "tiling path" of overlapping large clones (a set of clones, primarily bacterial artificial

chromosomes, which overlap and extend from one end of each chromosome to the other), and then sequencing those large clones by fragmenting them and cloning them in smaller pieces; the final challenge was to assemble the data based upon the physical map. The public genome project put sequence data into the public domain as they were generated and made the data available to all through the Internet, along with tools to allow analyses. This allowed scientists to use the data in real time and accelerated progress in many areas of genetic research. A competing private project by Celera Genomics developed a "whole genome shotgun approach" that involved fragmenting the genome into pieces of different sizes, sequencing both ends of the cloned fragments, and assembling the data computationally based in part on the known distance between paired reads. The competition stimulated an earlier than expected completion of the project. The human genome was declared completed in April 2003, the 50th anniversary of the determination of the structure of DNA by James Watson and Francis Crick.

Researchers now have the sequence of nearly all of the three billion base pairs that make the haploid human genome, although some repetitive regions are missing due to technical issues. The reference human genome sequences—both from the public project and from Celera—are mosaics, each derived from several individuals. Since then, new techniques and strategies have allowed sequencing of the diploid genome of some individuals, which has revealed additional sequences and some structural variations. A new target is to develop technology that permits the sequencing of individual genomes at low cost.

Understanding the genome and annotating the sequence is a major project that will take many more years. The data have already provided surprises, such as finding that there are fewer than 25,000 human genes (although there are disagreements about how to recognize and count genes). More recent studies, enabled by the genome sequence, have shown that alternative splicing (whereby different forms of messenger ribonucleic acid [mRNA] are produced from the same DNA template, leading to different protein products) is far more widespread than initially thought and generates a much greater number of proteins from this small number of genes. The fact that a small number of genes can lead to the great complexity that characterizes the human species suggests that gene regulation at both transcriptional and post-transcriptional levels plays a crucial role in the development and maintenance of an organism.

Many new genes have been identified from the genome sequence, and families of genes have been recognized. There is much work remaining, including discovering the function of the vast majority of the DNA, which does not code for proteins. Comparative genomics, in which genome sequences from other organisms are determined, is an important tool in this effort. Comparing these genomes to each other and to the human genome is contributing greatly to the task of recognizing new genes and understanding the function of the sequences.

Evolutionary conservation is one way to recognize functionally important sequences. The original design for the genome project included sequencing genomes of the five model organisms listed above as tests of the methods, to assist research on these widely studied organisms, and for comparative analyses. Comparative genomics has been greatly enhanced by the tremendous drop in the cost of sequencing that resulted from the genome project, and many additional genomes have been sequenced. As of April 2008, 464 eukaryotic genome sequencing projects were completed or underway. Information on these can be found online at the National Center for Biotechnology Information: National Institutes of Health Web site.

Another extension of the Human Genome Project has been the search for genetic variability among humans. An international effort called the HapMap project has discovered millions of positions in the genome that differ from one individual to another. Genomes of many individuals are now being sequenced in whole or in part in the "1000 Genomes Project" to discover more genetic variations, including variations in the number of copies of some regions. These data are important for projects designed to find genetic variations that are related to the risk for diseases.

Complex diseases, including alcohol and drug dependence, result from the interplay of genetic variation and the environment. No two individuals, except identical twins, have exactly the same genome sequence. In fact, there are more than six million differences between a pair of randomly chosen individuals. While many of these variations have no functional

significance, some affect the sequence of proteins or the regulation of their expression. The reference sequences, catalogs of variations, and technologies to measure these variations that resulted from the Human Genome Project have tremendously aided the search for the variations that affect disease.

See also **Risk Factors for Substance Use, Abuse, and Dependence: Genetic Factors.**

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GERMANY. In the geographic area that became Germany, tobacco entered society first and foremost as an addition to the pharmacopoeia in the sixteenth century. Its recreational use was frowned upon and restricted through legislation, and many German states issued edicts against smoking throughout the eighteenth century. Despite this, smoking (mostly pipe smoking) spread, paralleling a rise in drinking. Prior to the nineteenth century, the most popular alcoholic beverage was beer. Distilled spirits were the preserve of wealthier sections of society or used for festive occasions. After the Napoleonic wars, however, disastrous harvests limited the grain available for beer production. The potato provided a substitute and, with depressed agricultural conditions, there was a surplus of potatoes that could be converted to spirits. Between 1806 and 1831, the consumption of spirits tripled, becoming widespread among the laboring poor. There was a close connection between inadequate nutrition and drinking, as spirits provided a source of calorific energy. There was also a popular perception that alcohol had medicinal properties.

Between 1855 and 1873, per capita consumption of spirits increased nearly 50 percent, while that of beer doubled. This increase was a result of rising real incomes during the Industrial Revolution. Alcohol was one of the few consumer goods available to the lower classes at the time. The consumption of tobacco also rose, particularly as cigars became popular. By 1878 there were just under 4,000 cigar manufacturers in Germany. These were small-scale, family-owned businesses, and production was labor intensive. The main types of tobacco consumed were heavier Oriental tobaccos; consumers were male; and cigars were everyday, as opposed to luxury, items.

The turn of the twentieth century saw the cigarette grow in popularity as a result of mechanized production. This growth threatened to overtake cigar consumption, and the German government sought to protect the labor-intensive cigar industry through differential taxation. In 1906, cigarettes became subject to a revenue seal (meaning that an additional duty had to be paid), following the imposition of a similar revenue seal on *sekt* (sparkling wine) in 1902. Taxation underwent various changes during the First World War and the Great Depression of the 1930s, but cigars remained more favorably taxed than cigarettes. Thus, cigar consumption maintained parity with cigarette consumption until after the Second World War. In 1938, 36.8 percent of tobacco was made into cigars, 34.9 percent into cigarettes, and 28.3 percent into other tobacco articles.

HOSTILITY TO SMOKING AND DRINKING

Beginning in the 1820s, increased alcohol consumption among the laboring poor gave rise to middle-class fears about drunkenness. The temperance movement began in America but spread across Britain and through the Protestant states of northern Germany as part of a wave of religious revival, which fitted within *Bürgertum* (bourgeoisie) ideals of self-help through personal discipline. The first German temperance

association was formed in 1830 in Hamburg. An estimated 600,000 adult men took the pledge by 1846, and more than 1,250 organizations were founded. The 1848 revolutions saw a decline in the popularity of temperance, however, as other social causes became more dominant. Further, poor harvests in 1846 and 1847 limited supply and made alcohol more expensive.

The temperance movement reemerged in the 1880s, following concerns about the pervasive nature of drinking in working-class life. There were also sporadic publications against smoking. In 1910 the *Bund Deutscher Tabakgegner* (Alliance of German Anti-Tobacconists) was established through an amalgamation of earlier German-language antismoking organizations. Critics saw youth smoking and drinking as a particular threat, for young people were not seen to be developed enough to tolerate nicotine, while drinking was seen as a sign of waywardness. Antismoking movements were overshadowed by anti-alcohol movements, but both merged with ideologies of racial and social hygiene. Proponents of hereditary theories correlated alcohol with degenerative diseases, criminality, and prostitution. Such beliefs led to calls for the compulsory sterilization of alcoholics.

In 1934, the main German agency against alcoholism, the *Deutsche Reichstelle gegen den Alkoholismus*, became part of government efforts to fight addiction, and in 1939 the *Reichstelle gegen die Alkohol und Tabakgefahren* (Reich Agency against the Dangers of Alcohol and Tobacco) was formed by the National Socialist regime. Here, the aims of the anti-alcohol and the antismoking movements coalesced with Nazi ideology, and the *Reichstelle gegen die Alkohol und Tabakgefahren* issued propaganda against smoking and drinking. In addition, many states passed legislation prohibiting youth smoking. The government funded smoking research, building on the first studies linking smoking with lung cancer in the late 1930s. Measures against alcoholics were more sinister, with the creation of a register of alcoholics, compulsory sterilization under the 1933 Sterilization Law, and some alcoholics being sent to concentration camps. By the early 1940s the regime had shied away from antismoking measures because of tobacco shortages and the hostility that the restrictive measures aroused. Anti-alcohol campaigns also had little success, and consumption rose throughout the period.

CHANGES IN ADDICTIONS AFTER THE SECOND WORLD WAR

After the Second World War, the tobacco market underwent a drastic change due to shortages of German and Oriental tobacco and the availability of American cigarettes through the black market. Within five years, West German tastes had changed toward lighter Virginian cigarettes, which assumed prominence in the market. From the 1950s onward, per capita consumption, particularly of cigarettes, grew annually. For health reasons, filter cigarettes were particularly popular, and by 1956 around half the smoking population had switched to a filtered brand. Through the 1950s, around 10 percent of population income was spent on alcohol and tobacco, with the larger proportion of this money being spent on alcohol.

The West German government followed a relatively liberal line on smoking and drinking, believing it was up to adults to make decisions about their own consumption. The government therefore focused its attention on young people. In the 1950s, with increased disposable income and more freedom, the proportion of young people smoking increased to over half of the young men and 15 percent of the young women in the nation. This increase was seen by youth protection agencies as a psychological reaction to the trauma of the immediate postwar period and the breakdown of the traditional family, for many men were either killed or took several years to return from POW camps. The *Deutsche Gesundheitsmuseum* issued two booklets on the dangers of smoking in the 1960s, as well as a film, *Der Tod gibt eine Party* (Death gives a Party), which aimed to shock.

Drinking was also seen as a problem. With the inception of the *Bundeszentrale für Gesundheitliche Aufklärung* (BZgA, the Federal Agency for Health Education) in 1967, more funding became available for health education, and campaigns against smoking and drinking intensified. Television advertising of cigarettes was stopped in 1970 on a voluntary basis by the tobacco companies, although the subject of press and poster advertising remained hotly debated until 2006, when Germany finally adopted an EU resolution prohibiting tobacco advertising. For much of the second half of the twentieth century, the German government maintained a close relationship with the tobacco industry, which was generally held to have stalled progress in

promoting antismoking policies. The early twenty-first century has seen tax increases and moves toward restricting smoking in public places.

DRUGS

In contrast to the use of alcohol and tobacco, drug use in West Germany began to assume its current dimensions only in the early 1970s, when the "drug wave" occurred. This "wave" came in the wake of an increase in the use of cannabis, speed and heroin during the mid- to late 1960s. Previously, drug use had been most apparent in those with a therapeutic addiction to morphine, and in the cocaine use that was part of Weimar nightlife. The postwar expansion of drug use in West Germany emerged from two social trends: (1) the growth of the nation's youth as a distinct cultural category due to increasing financial independence, and (2) increased mass consumption, particularly of so-called *Genußmittel* (luxury goods), such as alcohol and tobacco.

The drug scene in West Germany emerged later than in other Western countries, but it was shaped by the same forces: rock and roll, unprecedented disposable income, and a context of international cultural exchange. The development of a drug "scene" varied from city to city and from region to region. Throughout the nation, "beat clubs" dominated as places where young people could congregate away from adults and listen to music from the United Kingdom and the United States, as well as from Germany. In Hamburg, the key area was along the Reeperbahn; in Berlin it was the Kurfürstendamm; in Munich, the Nikolaiplatz. A contributing factor was the disaffection some young people felt with postwar affluence and capitalism. These were the so-called *Gammler*, or "drop outs," who drifted from city to city, or country to country, seeking new experiences, smoking hashish, and using LSD. West Germans traveled in search of an alternative lifestyle and immigrants entered West Germany in search of a better standard of living, and this increased travel and tourism opened up drug routes from the Far East.

By the early 1970s, amid a climate of public fear about drug use, the authorities rushed through amendments to *Betäubungsmittelgesetz*, the main law dealing with drug trafficking and use. These amendments increased the sentences for the trafficking and posession of drugs to three years, and for major offenses the penalty increased to ten years; in 1983 the maximum penalties were increased to four years and fifteen years, respectively. The medical profession supported punitive measures against drug use, as did the police and youth protection agencies. Nonetheless, a rapid growth in drug use occurred throughout the 1970s and 1980s. By 1989 it was estimated that around 100,000 people were regular drug users. The main problem had become heroin, however, rather than cannabis and LSD. In addition, the space occupied by the drug scene expanded. In 1987, for example, Frankfurt's downtown drug scene covered a square mile and involved over 5,000 people dealing and using drugs.

In the late 1960s and 1970s, drug use, like smoking and drinking, was seen primarily as a youth protection issue. As well as penalizing drug use, the government, through the BZgA, funded and ran health education programs. The goal of such campaigns was to raise awareness of drug misuse, but the drug problem was clearly set in the context of wider patterns of deviant behavior and seen to be a failure of upbringing. Campaigns not only targeted young people, but also those with a responsibility for their education and upbringing. Adults were addressed in their capacity as drug consumers (of alcohol, tobacco, and over-the-counter pharmaceuticals), and the consequences of their own drug use was brought to their attention. Thus, problematic drug use was conceived and addressed in broad terms by targeting addiction in general, rather than one drug in particular. Young people were also targeted through popular culture. The youth magazine *Bravo* carried educational articles on drug use, commenting in a January 4, 1971, article titled "Tödliche Träume" ("Deadly Dreams") that "ever more young people are sucked into the drug wave," and warning, through teenage examples, of the dangers of hash and LSD. The magazine also set up advice centers in major cities.

The focus of intervention changed in the 1980s with the appearance of HIV infection among intravenous drug users. HIV/AIDS threatened the general public, as well as the users, and (as in other countries) this forced a paradigmatic shift in health policy. The threat of HIV led to a policy of harm reduction, with less emphasis on punitive legislation.

Needle-exchange programs began in the mid-1980s, providing and delivering clean needles to users, and "injecting rooms," also known as "health rooms," were established to provide a clean and safe environment for drug injection. These were initially clandestine operations, but they were legalized in 1999. Further, by the 1990s, methadone substitution programs had been put in place to combat the dangers from black market and potentially adulterated drug use. Such substitution programs initially faced political opposition, but by 1995 over 1,000 drug users in Frankfurt were participating in a methadone program, and these programs expanded in urban centers. From 1984 onward, the number of drug-related deaths declined, though they began to rise again in 2007. The use of drugs such as methamphetamine and cocaine also increased, and by 2008 around 200,000 people were using opiates, cocaine, amphetamines, and hallucinogenics.

By 2008, the focus of concern about addiction had shifted back to alcohol. The annual drugs report (*Drogen und Sucht Bericht*, 2008, published by the Bundesministerium für Gesundheit) noted a decrease in the number of young people using cannabis and tobacco, but it also reported an alarming rise in alcohol consumption, binge drinking, and the number of hospital admissions from alcohol poisoning, particularly among young people. Around 600,000 people, mostly young people, were found to be regular cannabis users, but fewer were taking up the substance. Smoking also declined among young people, from 28 percent to 18 percent between 2000 and 2007. In 2008 the German government was preparing a national campaign against alcohol consumption, with a particular focus on the nation's youth.

See also **Alcohol: History of Drinking in the United States; Alcohol: History of Drinking (International); Club Drugs; European Union; Foreign Policy and Drugs; Injecting Drug Users and HIV; International Drug Supply Systems; Temperance Movement; Tobacco: An International Overview.**

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ROSEMARY ELLIOT

GINSENG. Ginseng is the most revered and well-known plant of Chinese herbal medicine; it is sold over the counter in Asian apothecaries and groceries worldwide. This plant of the family Araliaceae grows on both sides of the Pacific, with *Panax schinseng* the Asian form and *Panax quinquefolius* the North American form. It is a perennial herb with five-foliate leaves, and its fleshy aromatic root is valued as a tonic and a medicine.

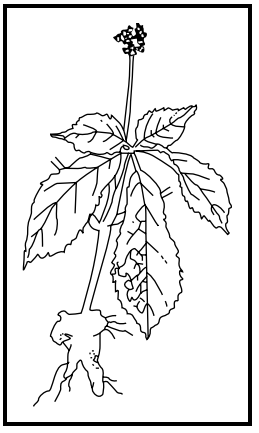
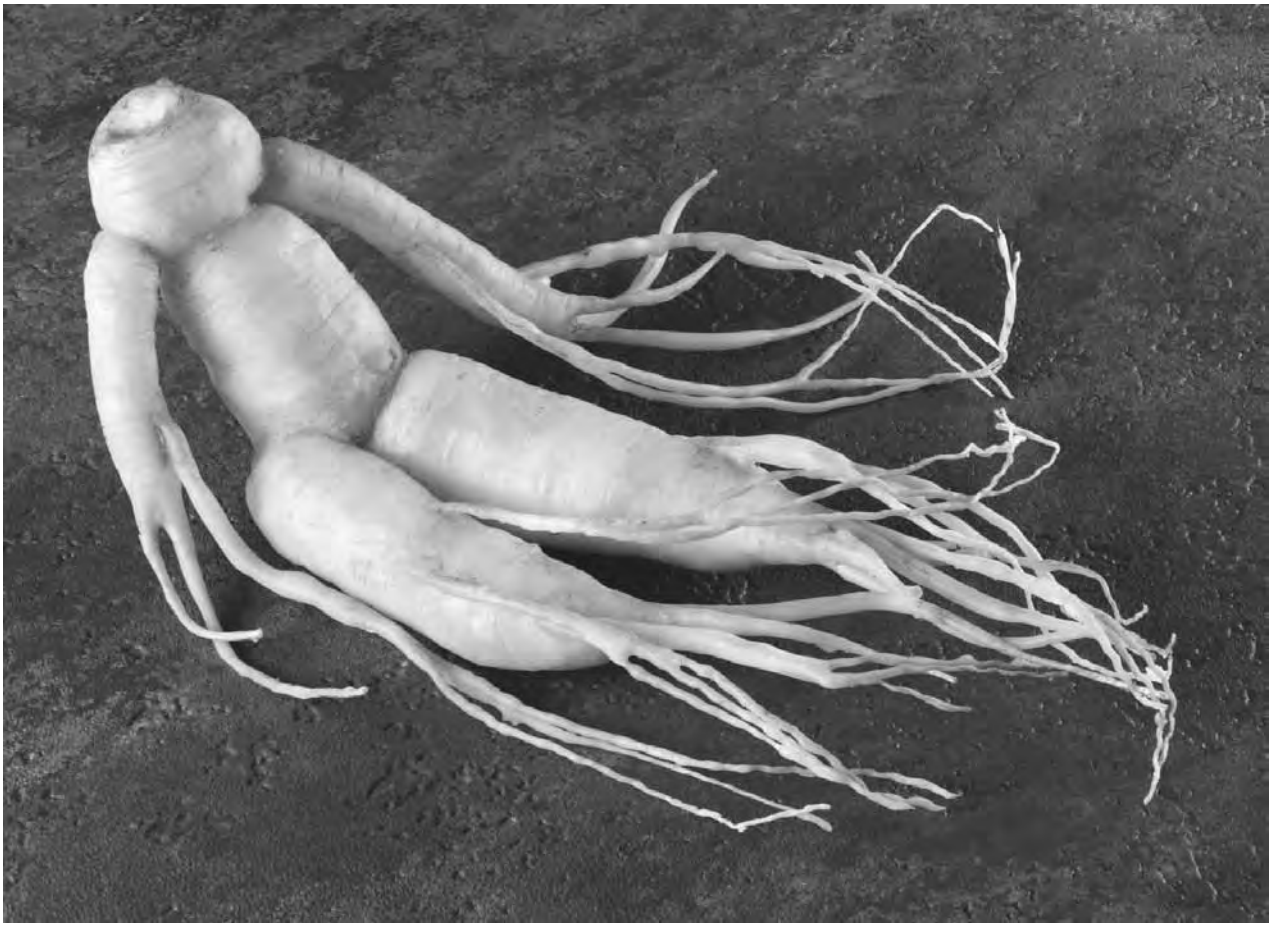


Figure 1. Ginseng. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING



Ginseng root. FOODFOLIO/ALAMY.

The root has been used by Native Americans, Siberians, Chinese, and other Asians for millennia. Usually it is taken as a tea—once a day as a general preventative tonic, more frequently for therapeutic purposes. Since the North American form is considered the most potent, it is now grown in Asia along with the local variety. American ginseng is also exported to Asia, then sometimes reimported into the United States as a Chinese or Korean herbal. Both the wild and cultivated forms are used. Roots older than five years are needed for good effect, and the older and larger the root (seven to fifteen years is prized), the more the ginseng costs. Dried roots are heated and sliced thinly to make tea, but pieces may be kept in the mouth, sucked, and eaten. The many ginseng products now sold (sodas, candies, etc.) have no real tonic or therapeutic value.

Ginseng has a bittersweet aromatic flavor, contains alkaloids, and is said to be good for mental arousal and general well-being. It has not been established in Western medicine and pharmacology, although it contains properties that might be isolated and used pharmacologically.

See also **Plants, Drugs From.**

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GLUTAMATE. Glutamate (GLU) is a dicarboxylic aliphatic amino acid, the chemical symbol for which is $COOH\text{-}CH_2\text{-}CH_2[NH_2]\text{-}COOH$. It

is abundant in all cells of the body. In many neurons (nerve cells) glutamate is packaged into synaptic vesicles and serves as an excitatory neurotransmitter in the brain. Once released as a transmitter, glutamate binds to both ionotropic (containing an ion channel) and metabotropic (signaling through intracellular second messengers) receptors and is removed or sequestered by a high-affinity uptake system that transports glutamate into both neurons and glia. As the primary excitatory neurotransmitter in the brain, glutamate, along with other neurotransmitter systems, regulates most behaviors, including emotional and cognitive perceptions. Accordingly, a role for glutamate has been proposed in a variety of pathologic conditions, ranging from schizophrenia and addiction to Alzheimer's and Parkinson's diseases. Consequently, developing drugs that regulate glutamate neurotransmission has become a high priority. Drug development is focusing on agonists and antagonists at glutamate receptors. In addition to neuronal receptors, it is now clear that release and elimination of glutamate by glial cells (non-neuronal cells that serve a variety of brain functions) represents a critical homeostatic function in regulating glutamate neurotransmission. These mechanisms are also emerging as targets for medications to treat brain-related disorders.

See also **Dopamine.**

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PETER W. KALIVAS

GLUTETHIMIDE. Glutethimide was introduced into clinical medicine in 1954. It was prescribed to treat insomnia and sold as Doriden. It was first acclaimed as a safer "nonbarbiturate" hypnotic—implying that it was free of the problems of abuse, addiction, and withdrawal that were, by then, recognized drawbacks of the older barbiturate sedative-hypnotics. Within ten years, however, it was recognized that, in most respects, its actions are like those of the barbiturates and it shares the same disadvantages.

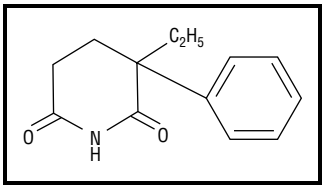

Figure 1. Chemical structure of glutethimide. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Glutethimide is structurally related to the barbiturate drugs and, like the short–acting barbiturates, it depresses or slows the central nervous system. Side effects from its proper use are relatively minor, but a rash is often seen. Like barbiturates, it can produce intoxication and euphoria; tolerance and dependence can result with daily use. Glutethimide is metabolized somewhat differently than barbiturates, and overdose is often far more difficult to treat than barbiturate overdose; fatalities are not uncommon. As a consequence of this and its abuse potential, glutethimide is included in Schedule III of the Controlled Substances Act. Since the introduction of the benzodiazepines to treat short–term insomnia, the use of glutethimide has decreased considerably.

See also **Barbiturates; Sedatives: Adverse Consequences of Chronic Use.**

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GOLDEN TRIANGLE AS DRUG SOURCE. Opium, the sap of the opium poppy (*Papaver somniferum* Linnaeus), is a bitter, brownish, and sticky substance. This alkaloid-rich and addictive narcotic drug has been known to humanity since time immemorial. Between the early 1950s

and the early 1990s—that is, before Afghanistan's opium production surpassed that of Burma—most of the world's illicit opium originated in the so-called Golden Triangle, the name given to the area of Mainland Southeast Asia known for its large illicit opium production. (The Union of Burma was renamed "Myanmar" on June 25, 1989, by the military dictatorship then known by the acronym SLORC [State Law and Order Restoration Council]. This name change was recognized by the United Nations and a number of countries, including France, but not by others, such as the United Kingdom and the United States.)

The Golden Triangle is located in the highlands of the fan-shaped relief of the Indochinese peninsula, where the international borders of Burma, Laos, and Thailand intersect. Opium poppy cultivation has taken place in the border regions shared by the three countries since the mid-nineteenth century, and it developed considerably beginning in the 1950s. However, this production receded markedly in the 1990s, and it is now confined to the Kachin and Shan States of northern and northeastern Burma, along the borders of China, Laos, and Thailand.

ABOUT THE GOLDEN TRIANGLE

The Golden Triangle is not only an isolated mountainous and heavily forested area overlapping the contiguous and outlying border areas of three countries, it is also populated by many extremely diverse ethnic groups, many of them tribal and semi-nomadic slash-and-burn agriculturalists. In fact, the international borders of Burma, Laos, and Thailand also cut across two zones that are intricately woven together: the Tai linguistic zone, composed of Shan, Thai, and Lao peoples, over which is superimposed a more complex zone of numerous other ethnic groups that are dispersed throughout the three-border area and in neighboring China.

The term *Golden Triangle* was coined by the Assistant Secretary of State Marshall Green of the United States during a press conference on July 12, 1971. Referring to a polygon whose angles could be found in Burma, Laos, and Thailand, where opium production was indeed concentrated, Green implicitly acknowledged (and probably rightly so) the absence of large-scale commercial opium production in China. Once the world's main opium producing country, China drastically reduced poppy cultivation and opium trade after the Communist victory in 1949. Green's exclusion of China from the so-called Golden Triangle was all the more necessary because it was made three days prior to the announcement by President Richard Nixon of his official visit to the People's Republic of China in February 1972. This was the first visit of a U.S. president to Communist China.

In addition to being a politically grounded geographic reference, the term *Golden Triangle* also refers to one of the region's most important economic features: opium production. Mainland Southeast Asia became a major source of opium over the course of the second half of the twentieth century. According to the Swedish journalist and veteran Burma-watcher Bertil Lintner, the first traders in the three-border region—especially those of the Thai-Burmese border towns of Mae Sai (northernmost Thailand) and Tachilek (Shan State, eastern Burma)—reportedly exchanged the precious substance for 99 percent pure gold ingots. Such reports inspired the name, Golden Triangle.

TRENDS IN POPPY CULTIVATION AND OPIUM PRODUCTION

Opium production in Mainland Southeast Asia has always been concentrated in the three-border region, where rugged hills and mountains, heavy monsoon rains, and a lack of transportation infrastructure have long protected rebel armies and illicit crops from the writ of central governments and national and international antidrug agencies. Yet after decades of expansion of poppy cultivation in the three countries, opium production has progressively receded—it almost completely disappeared from Thailand in the 1990s, and it seriously decreased in Laos during the early 2000s. Poppy cultivation has diminished, concentrating in northern and northeastern Burma, where it had originated in the mid-nineteenth century. Although Burmese opium production has also considerably decreased since 1998, it has nevertheless proven to be extremely geographically and historically resilient.

Burma's turbulent political history since its independence from Britain in 1948 can clearly be held responsible for Asia's longest illicit opium production. The opium economy and the war economy have clearly nurtured one another in a

country that has suffered an internal war for over sixty years (the Karen National Union [KNU] has fought Burma's central government since the country's independence). Indeed, as an extremely valuable economic resource, opium has often enabled warring factions to fund their respective war efforts. Opium production has also weighed upon strategic negotiations, offering both state and nonstate actors opportunities to gain political leverage or create ad hoc strategic alliances. For instance, the Burmese government has continually integrated opium into its negotiation strategy so as to affect power struggles, something that some antigovernment forces have directly or indirectly benefited from.

Yet Burma's opium production progressively decreased between the mid-1990s and the mid-2000s, dropping from a record of 1,791 tons in 1993 to only 315 tons in 2006, according to the United Nations Office on Drugs and Crime. But production surged to 460 tons in 2007, mostly as an economic consequence of hasty and uncompensated opium bans. In fact, opium production in Burma abated not as a result of central government policies but as a consequence of bans issued by the leaders of three of the private armies controlling the country's largest opium-producing areas: Shan State's Special Region 4 (Mong La) in 1997, Special Region 1 (Kokang) in 2003, and Special Region 2 (Wa) in 2005. Yet opium is still produced in Burma, the world's second largest illicit opium producing country after Afghanistan (in 2007, Afghanistan produced 8,200 tons, 18 times more than Burma). In the mid-2000s, Burmese opium is still mostly produced in southern Shan State, where poppy acreage has increased in 2005, 2006, and 2007, when 65 percent of Burma's poppies were cultivated in South Shan State and 25 percent were cultivated in East Shan State. Parts of Kachin State and Kayah State also produce opium in significant quantities. In 2007, after years of decline, the overall Burmese opium production increased by 46 percent, due to higher yields than in 2006 and a 29 percent increase in opium poppy cultivation.

METHAMPHETAMINE PRODUCTION

While opium production ebbed in Burma from the mid-1990s on, methamphetamine production quickly developed, especially in Shan State. Methamphetamine is a synthetic drug that is classified as an amphetamine-type stimulant (ATS). It is known as *yaa baa* ("madness drug") in Thailand, where consumption developed considerably after the mid-1990s and especially in the early 2000s. During this period, between 500 and 800 million *yaa baa* pills were reportedly produced on a yearly basis in Burma. These pills were then trafficked to consuming countries such as Thailand and China.

In November 2000, the head of the Thai National Security Council identified drug trafficking as the major threat to Thailand's national security. Various Thai officials blamed the situation on neighboring Burma and denounced Rangoon's "narcotic aggression" against Thailand. *Yaa baa* seizures doubled between 1996 and 1997 (to 1.5 tons), between 1997 and 1998 (to 2.8 tons), and again in 1999 (to 4.5 tons). During the same period, heroin seizures declined by almost 30 percent, with only 511 kilograms confiscated in 1998. This increase in *yaa baa* trafficking coincided with an increase in violence along the Thai-Burma border, where numerous incidents of varying intensity led to major crises between the two countries.

Upon taking office in February 2001, Thailand's prime minister, Thaksin Shinawatra, vowed to prevent and suppress both drug trafficking and drug consumption in the kingdom. On February 1, 2003, he launched a nationwide "war on drugs" aimed at making the country drug-free within three months. His government crackdown resulted in the seizure of 40 million *yaa baa* pills; the arbitrary arrest of 92,500 drug addicts, 43,000 dealers, and 750 drug producers and importers; and the unexplained killing of more than 2,500 persons. Although the Thai government claimed that the operation had been a "victory beyond expectation," Thaksin called for a second "war" in October 2004. Of course, in 2008, methamphetamine trafficking and consumption had not disappeared from Thailand. In fact, the trend was in the opposite direction, as the 2008 launch of a new "war on drugs" indicates.

DRUG TRAFFICKING ROUTES OF MAINLAND SOUTHEAST ASIA

Since the emergence of the Golden Triangle, opiate trafficking has followed the main caravan axes of Southeast Asia and southern China. Indeed, Chinese opium was already being exported to Southeast Asia at the end of the nineteenth century, when Chinese production was double the amount of

imports forced onto the Chinese Empire by the British. The Haw (Chinese Muslims), the Hmong, and the other tribal populations who migrated from China to Southeast Asia played an important role in spreading opium production in the Indochinese peninsula, and they had a positive impact on the emergence of the Golden Triangle by perpetuating a few trafficking and contraband routes. The caravan tracks of the Haw, which crisscrossed Siam (modern-day Thailand) very early, played a large role in turning Thailand into a privileged hub of heroin trafficking after World War II.

Thailand remained the main heroin trafficking route in Southeast Asia until the early 1990s. However, a number of factors have contributed to the reorientation of drug trafficking routes within Southeast Asia, and to the development of new routes to other parts of the continent. The Thai crackdown on heroin trafficking that took place after the 1984 nationwide opium eradication campaign considerably reduced the use of its well-developed road system by smugglers and traffickers from the Thai-Burma border. Subsequent patrols of the northern and northwestern Thailand borders by the Thai Third Army and the Border Patrol Police also disrupted the routes across the Thai-Burma border used by opium and heroin traffickers. While China is now certainly the main transshipment destination for heroin from Burma, it is not the only one, as northeast India also draws some of the traffic.

In the late 1990s, the diversification of drug trafficking routes increased, as did the diversification of illicit drug production. The explosion of methamphetamine production in Burma has led to a resurgence in use of the Thai route, for Thailand is by far the first consumer market of *yaa baa* in the region. *Yaa baa* traffickers differ from others in that they are more numerous and carry small quantities of pills across the Thai-Burma border. They form what Thai authorities have referred to as an "ant army," crisscrossing the border along countless hill paths and using small tribal villages as staging posts. The strong crackdown led by the Thai army and police in the early 2000s in the northernmost part of the country has recently diverted the flux of methamphetamine, pushing traffickers to use new itineraries.

The roads of Laos are frequently used for transporting illicit drugs bound for Thailand, even though drug trafficking aboard speedboats along the Mekong River—which demarcates the international border between the two countries—is the first choice. Further south along the Thai border and lower on the Mekong, Cambodia is also increasingly used as a staging point for trafficking methamphetamine into Thailand. Vietnam has similarly been turned into a drug trafficking route, either from or to China; overseas trafficking is frequently organized from Vietnamese seaports. While most (80%) of the drugs entering Thailand still allegedly come across the northern part of the Thai-Burma border, the constant strengthening of Thai antidrug actions has clearly fostered a wide diversification of drug trafficking routes, as well as a diminution of the quantity of drugs being transported at any one time.

See also **Crop Control Policies; Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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PIERRE-ARNAUD CHOUVY

HAIR ANALYSIS AS A TEST FOR DRUG USE. Because every drug taken becomes a permanent part of the user's hair, laboratory analysis of hair can reveal the presence of a variety of drugs including opiates, cocaine, amphetamines, phencyclidine, marijuana, nicotine, and barbiturates. Hair analysis is widely used and accepted by courts, law enforcement bureaus, and government agencies. It is used for a variety of purposes including employment screening, determination of maternal or fetal drug exposure, and validating self-reports of drug use (Kintz, 1996; Harrison & Hughes, 1997).

Unlike urinalysis, which can only detect comparatively recent drug ingestion (e.g., depending on the drug, between days and weeks), hair analysis can reveal the ingestion of drugs during the past ninety days or even longer. Because head hair grows at a relatively constant rate of one-half inch (1 cm) (1 inch = 2.54 cm) per month, segmental analysis of hair strands could localize the period of drug exposure to within as little as one particular week. Although various hair treatments such as tinting and perming may affect test readings, detectable traces are indelible in the hair (Kintz, 1996).

DRUGS IN HAIR

Hair is nonliving tissue composed primarily of a sulfur-rich protein called keratin. Hair grows from the follicle (a saclike organ in the skin) at a rate of 0.3 to 0.4 millimeters (0.011 to 0.012 inches) per day in cycles of active growth followed by a resting phase. For an adult, approximately 85 percent of scalp hair is in the growing stage at any time. Two sets of glands are associated with the follicle: the sebaceous glands, which excrete sebum (a waxy substance), and the apocrine glands, which excrete an oil that coats the hair. Hair color is determined by genetic programming for varying amounts of melanin, a pigment that is synthesized in hair cells called melanocytes.

Although the exact mechanism by which drugs and drug metabolites are incorporated into hair is still unknown, they enter into hair by multiple processes. Drugs and drug metabolites may be deposited from the capillaries, which supply blood to the follicles, or they may be excreted in the sebum, oil, or sweat that coats the hair shafts. Drugs can also be deposited on the hair by environmental exposure (such as marijuana smoke or cocaine powder in the air) (Kintz, 2008).

When hair is analyzed for drug use a sample is taken from either the head or another part of the body. It's washed to remove dirt and any external drug deposits (the wash medium is also tested) then stripped of melanin. The actual analysis is performed by radioimmunoassay, which detects not only traces of drugs but their metabolites, breakdown products that appear only when the body has metabolized the drug. All positive samples are confirmed by gas chromatography/mass spectrometry (GC/MS). This second test has a cutoff level to eliminate specimens containing drug levels that could come from environmental exposure such as inhaling second-hand marijuana smoke or eating food that contains poppy seeds (Kintz, 1996).

SIGNIFICANCE OF HAIR DRUG TESTING

Once a drug is embedded in hair it appears to be stable indefinitely although its concentration diminishes somewhat over time. Cocaine metabolite, for example, has been detected in hair from a pre-Columbian mummy more than 500 years old. This is an obvious advantage over other methods of drug testing such as urinalysis, which can detect drugs ingested only within the past few days or weeks. Depending on the length of the hair, analysis can determine that drug use has occurred from months to years. Hair is also easily collected and stored. If more testing is required another sample may be easily obtained. One disadvantage of hair analysis is that it will not reveal drug use during the three to five days before testing since hair does not grow quickly enough to show this. Urine testing can thus be used to complement the results of hair analysis. Hair analysis is also more expensive than urinalysis and the results take longer to be determined.

CONTROVERSY

Hair drug testing techniques have been greatly improved over time. However, quantitative detection of some drugs and their metabolites—particularly THC, the major active component of cannabis—is still considered difficult (Uhl & Sachs, 2004).

Some groups have raised concerns that hair testing may be biased against minority populations such as African Americans. Multiple cross-comparison studies between self-report and hair testing on cocaine demonstrate discrepancies to be correlated with hair color (Ledgerwood et al., 2008). A number of in vitro experiments show that hair samples from different gender and racial groups incorporate differing amounts of drugs under identical conditions (Kidwell et al., 2000). Hair testing labs claim that their processes, which remove melanin from samples, eliminate any chance of distinction or discrimination by race or ethnic group. Combining urinalysis and hair testing may be needed to assess a more complete profile of the individual's past and present drug use for forensic and occupational applications.

See also **Industry and Workplace, Drug Use in; Military, Drug and Alcohol Abuse in the United States.**

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HALLUCINATION. The word *hallucinate* is derived from the Greek *halyein*, meaning "to wander in mind." Hallucinations are perceptions that occur in the absence of a corresponding external sensory stimulus. They are experienced by the person who has them as immediate, involuntary, vivid, and real. They may involve any sensory system, and hence there are several types of hallucinations: auditory, visual, tactile (e.g., sensations on the skin), olfactory (smell), and gustatory (tastes). Visual hallucinations range from simple (e.g., flashes of light) to elaborate visions. Auditory hallucinations can be noises, a voice, or several voices carrying on a conversation. In command hallucinations, the voices often order the person to do things that at times involve acts of violence.

Hallucinations have been a hallmark of mental illness throughout history. They are an important clinical feature of several psychiatric conditions in which psychosis can occur, such as schizophrenia, manic-depressive illness, major depression, and dissociative states. Withdrawal from alcohol can cause visual as well as other sensory hallucinations. In alcoholic hallucinosis, a person dependent on

alcohol develops mainly auditory hallucinations that can persist after the person has stopped drinking. Hallucinations may be induced by illicit drugs, such as cocaine, amphetamines, and LSD. These hallucinations are usually visual, but they can also be auditory or tactile, as in the sensation of insects crawling up the skin (an example of a haptic hallucination). Occasionally, after repeated ingestion of drugs, some people experience "flashbacks"—that is, spontaneous visual hallucinations during a drug-free state, often months or years later.

The cause of hallucinations is not known, but it is likely to be multifactorial through a combination of physiological, biological, and psychological variables. Numerous hypotheses have been proposed. According to a perceptual release theory, hallucinations develop from the combined presence of intense states of psychological arousal and decreased sensory input from the environment (e.g., sensory deprivation) or a reduced ability to attend to the sensory input (e.g., in delirium). This leads to the emergence of earlier images and sensations that are intepreted as originating in the environment. Other researchers suggest that abnormalities in brain cell excitability or in the information processing system of the central nervous system cause hallucinations. Biochemical theories implicate brain neurotransmitters such as dopamine. Drugs that block brain dopamine activity (antipsychotics) alleviate hallucinations, whereas drugs that stimulate dopamine release induce hallucinations.

Hallucinations can occur in people who are not mentally ill. In acute bereavement, some people report seeing or hearing the deceased. Sensory, sleep, food, and water deprivation can produce hallucinations, as can the transition from sleep to wakefulness and vice versa (called hypnopompic and hypnogogic hallucinations, respectively). These hallucinations can occur as side effects of prescribed medications, such as drugs that treat cardiac conditions, or in various medical disorders (e.g., migraines, Parkinson's disease, infections). They have been described in persons with hearing loss and blindness; in these instances, it has been hypothesized that they may be due to chronic sensory deprivation.

The treatment of hallucinations is part of the treatment of the entire psychotic syndrome. Antipsychotic medications (e.g., haloperidol, chlorpromazine) are effective in reducing and often eliminating hallucinations. When the hallucinations are part of a medical disorder, it is necessary to correct the underlying condition, or remove the causative agent, in addition to prescribing antipsychotic medication.

See also **Complications: Mental Disorders; Delirium Tremens (DTs); Hallucinogenic Plants; Hallucinogens.**

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MYROSLAVA ROMACH
KAREN PARKER

HALLUCINOGENIC PLANTS. Literally hundreds of hallucinogenic substances are found in many species of plants. For example, a variety of mushrooms contain indole-type hallucinogens, the most publicized being the Mexican or "magic" mushroom, *Psilocybe mexicana*, which contains both the hallucinogenic compounds psilocybin and psilocin, as do some of the other *Psilocybe* and *Conocybe* species. The peyote cactus (*Lophophra williamsii* or *Anhalonium lewinii*), which is found in the southwestern United States and northern Mexico, contains mescaline. The seeds of the morning glory, *Ipomoea*, contain hallucinogenic lysergic acid derivatives, particularly lysergic acid amide. Many of these plants and plant by-products were and are used during religious ceremonies by Native Americans and other ethnic groups.

Some plant substances may contain prodrugs, that is to say, compounds that are chemically altered in the body to produce psychoactive

substances. For example, nutmeg contains elemicin and myristicin, whose structures have some similarities to the hallucinogen mescaline as well as the psychostimulant amphetamine. It has been hypothesized that elemicin and myristicin might be metabolized in the body to form amphetamine-and/or mescaline-like compounds, but this has not been proven. The fact that hallucinogenic substances are found in nature does not mean that they are safer or purer than compounds that have been synthesized in the laboratory. Some common edible mushrooms that can be purchased in any supermarket may be sprinkled with LSD or other hallucinogens to be misrepresented as magic mushrooms. In addition, serious problems—even death—may occur when species of hallucinogenic plants are misidentified and people mistakenly ingest highly toxic plants, such as poisonous mushrooms.

See also **Ayahuasca; Ibogaine; Jimsonweed; Plants, Drugs From.**

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R. N. PECHNICK

HALLUCINOGENS. Hallucinations are audio, visual, and temporal distortions. Hearing or seeing things that do not really exist or feeling that time has slowed down, sped up, or ceased altogether are typical hallucinations. *Seeing* sounds, *hearing* colors, and perceiving that still objects are moving are other examples of hallucinations. Out-of-body experiences also may be considered hallucinations. Of course, these things actually do not happen, but are the result of chemical reactions that alter the way the brain perceives information from the senses. These reactions may occur naturally when an individual goes through periods of illness, pain, hunger, or fatigue. Hallucinations may be produced also through ingesting particular substances.

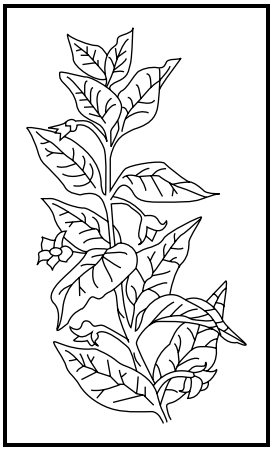

Figure 1. Belladonna. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Seeing pink elephants after drinking alcohol (though perhaps more appropriately associated with alcohol withdrawal) is an enduring image within U.S. culture. Inhaling large doses of marijuana or hashish may make users feel as if they were viewing the world through dream-like spectacles. Binge-use—whereby individuals consistently use drugs over several days without rest—of stimulants, such as cocaine (powder and crack) and crystal methamphetamine, has been associated with paranoia and delusions. Alcohol, heroin, and opiate withdrawal have also been linked with delirium. Even drinking excess cough syrup may cause the user to see, hear, or feel things that do not actually exist. While all of these substances may produce hallucinations, none is classified as a hallucinogen.

A review of the literature and Web sites indicates that hundreds of drugs, legal and illicit, natural and synthetic, are hallucinogens (Shulgin & Shulgin, 1991, 1997). An exhaustive review of these hallucinogens is beyond the scope of this entry. Rather, the focus here is on some well- and lesser-known hallucinogens that are consumed for recreational purposes—that is, for pleasure. These can be broken down into three rough categories: tryptamines, phenethylamines, and dissociative anesthetics.

TRYPTAMINES: LSD, PSILOCYBIN, AND DMT

Perhaps the most popular hallucinogens are LSD (lysergic acid diethylamide, commonly referred to as *acid*) and psilocybin *magic* mushrooms. These drugs fall under the category *tryptamine*. Recreational use of LSD and psilocybin was introduced widely into popular culture during the 1960s and 1970s, with LSD associated particularly with hippie counterculture (Yablonsky, 1968). Both drugs enjoyed a renaissance during the late 1980s and through the 1990s with the advent of underground rave culture (Sanders, 2006). Rave culture was commercialized across the United States in the 1990s and into the new millennium. Raves are dance parties where electronic dance music is played, often together with laser light shows, projected images, and artificial fog. During this same time period, rates of LSD and psilocybin use rose, particularly among young people (Hunt, 1997). The rise in popularity of raving and clubbing within popular culture and the reported increases in LSD and psilocybin among youth most likely influenced one another. The effects of LSD and psilocybin complement the rave/club atmosphere with its loud, bass heavy music, flashing lasers, disco lights, and colorful outfits worn by the clubbers (Sanders, 2006). To an extent, these drugs fit with this culture.

Another less well-known tryptamine, with a history of recreational use, is N, N-dimethyltryptamine, or DMT. DMT is one of the active ingredients in ayahuasca, a plant and bark mixture that has been used for sacramental purposes among people in South America for thousands of years and relatively recently among Westerners seeking novel psychedelic experiences (McKenna, 2004; Rushkoff, 1994). Hallucinations resulting from ingesting ayahuasca may be many hours long. In contrast, the hallucinations from using DMT by itself may be much shorter—perhaps 10 to 20 minutes depending on the dosage. The recreational use of DMT, whether organic or synthesized, dates back to at least the 1960s, when it was referred to

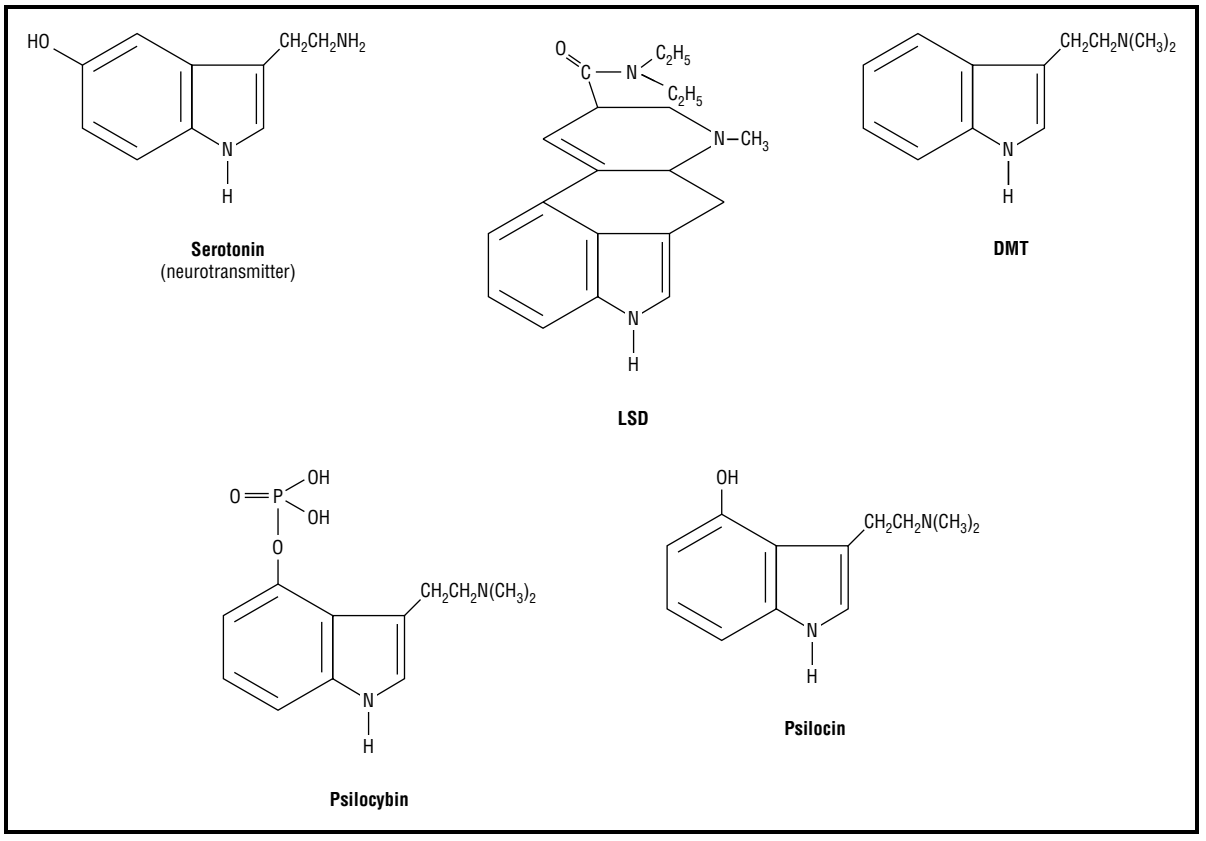

Figure 2. Indole-type hallucinogens. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

as "the businessman's lunch" because an individual could use the drug, feel its effects, and then return to a relatively normal state within a short time period, such as a lunch break (Halpern, 2004).

Other hallucinogens within the tryptamine family include alpha-methyltryptamine (AMT), diisopropyltryptamine, (DIPT), and their 5-methoxy (i.e., 5-MEO) counterparts (e.g., 5-MEO-AMT and 5-MEO-DIPT). Other tryptamines include N,N-dipropyltryptamine (DPT), N-isopropyl-N-methyltryptamine (MIPT), 4-hydroxy-N,N-diisopropyltryptamine (4-HO-DIPT), and many more (Shulgin & Shulgin, 1997). Similar to DMT, these drugs are dose-sensitive and are measured in milligrams, because tiny amounts may cause very powerful hallucinations lasting anywhere from 15 minutes to 24 hours or more. Very few accounts of these drugs have emerged within the research literature, though DMT and 5-MEO-DIPT, also known as *Foxy*, have been reported within rave and club culture (Sanders, 2006; cf. Measham, 2004).

PHENETHYLAMINES: MESCALINE, MDMA AND 2C-B

Other hallucinogens fall under the category *phenethylamine*. One relatively well-known hallucinogenic phenethylamine is mescaline. Mescaline occurs naturally in several types of cacti, but is most associated with peyote. Mescaline has a long history of recreational use, and reports of human use for sacramental purposes can be traced back millennia. Scientists in 2005 reported on the discovery of prehistoric peyote use in humans, dating to around 3700 BCE (El-Seedi et al., 2005).

MDMA is a stimulant-hallucinogenic phenethylamine. Commonly expressed feelings after using MDMA are empathy and euphoria; the street name of the drug is *ecstasy*. Ecstasy has been considered the club drug par excellence because of its tight association with rave and club culture (Shapiro, 1999; Sanders, 2006). Similar to LSD and psilocybin, the effects of ecstasy reportedly work well with rave culture environments. Moreover, prior to the emergence of raving in popular culture, ecstasy was relatively unheard of, so the rise of ecstasy use among youth has somewhat paralleled the rise of rave and club culture.

Other phenethylamines include hallucinogens within the *2C* series, such 2C-B (4-bromo-2, 5-dimethoxyphenethylamine), 2C-E (2,5-dimethoxy-4-ethyl-phenethylamine), and 2C-T-7 (2,5-dimethoxy-4-(n)-propylthiophenethylamine). Additional hallucinogenic phenethylamines are DOI (2,5-dimethoxy-4-iodoamphetamine) and DOB (2,5-dimethoxy-4-bromoamphetamine). Analyses of people's use of these drugs within the research literature are limited (Carmo et al., 2005). However, 2C-B, also

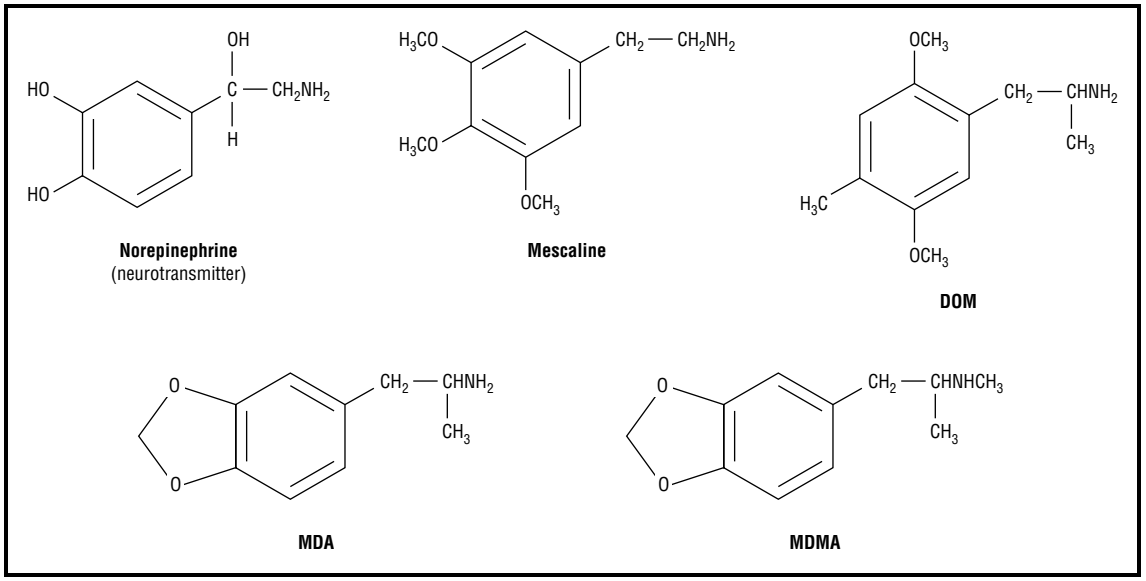

Figure 3. Substituted phenethylamines. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

known as *Nexus*, has been reported in rave and club culture (Sanders, 2006; Sanders et al., 2008), and qualitative experiences from users can be found on Internet Web sites (www.lycaeum.org; www.erowid.org). Reported dosages of these drugs are measured in milligrams, with the effects lasting up to several hours.

DISSOCIATIVE ANESTHETICS: PHENCYCLIDINE AND KETAMINE

Phencyclidine (PCP) and ketamine are chemically analogous substances that are considered dissociative anesthetics. Both were first designed for use as general anesthetics, and both can make users feel disconnected or detached from their bodies or their minds, which may include out-of-body experiences. Both PCP and ketamine use in humans was discontinued after adult patients described horrific nightmares and visions while sedated (Lankenau, 2006; Wish, 1986). Ketamine is used widely in veterinary practices, hence the street names of *cat* or *horse* tranquilizer in reference to the drug (Lankenau & Sanders, 2007).

PCP may come in liquid form, whereby users smoke cigarettes, *joints* or *blunts*, pre-soaked with PCP. PCP can also be used as a dry powder, suggesting a variety of other administrations (e.g., sniffing, injecting). PCP use has been linked with violence (Wish, 1986). Some academic findings, though, suggest the relationship between PCP use and violence may be overstated (Brecher et al., 1988; Hoaken & Stewart, 2003).

Ketamine has been considered a *club drug*, because of its association with rave and club culture, where it is often used with other drugs (Lankenau & Clatts, 2005). Using enough ketamine may produce what is referred to as the *K-hole*, distorted feelings of space and time and colorful visions (Lankenau, 2006). Ketamine may be administered intramuscularly—within a muscle—a relatively unique administration for any recreationally used substance.

LAWS AND POTENTIAL THERAPEUTIC VALUES

Certain hallucinogens are legal and may be purchased over the counter from particular shops in the United States as well as from businesses selling them on the Internet. One such drug is Salvia divinorum, a plant within the mint family. The psychoactive ingredient of the plant is called *salvinorin A* and is commonly sold under the name *Salvia* in extracts of various strengths.

In a report on the use of uncommon tryptamines and phenethylamines, youth purchased a variety of these drugs legally over the Internet where they were sold as "research chemicals" (Sanders et al., 2008; cf. Halpern & Pope, 2001; Kikura-Hanajiri et al., 2005; McCandless, 2004). Moreover, a variety of plants and fungi that naturally grow in the United States and that are legal to possess contain illegal substances that can be extracted (Halpern, 2004; McKenna, 2004).

Some tryptamines and phenethylamines have been illegal for many years, though other chemically analogous substances that produce roughly similar effects are not, for instance, tryptamine DMT. DMT is a Schedule I drug in the United States—the same legal status as heroin or crack cocaine—and is illegal to use. However, its chemical cousin, 5-MEO-DMT, is legal to use. Likewise, the phenethylamine 2C-B has been a Schedule I drug since 1994, but a related drug, 2C-I, may still be used legally. Under the Analogue Statute of the Controlled Substance Act, though, the trafficking of any substances chemically analogous to scheduled tryptamines and phenethylamines is illegal. In other words, while it remains legal to use 5-MEO-DMT, 2C-I and a host of other similar drugs, selling them is illegal.

Alexander Shulgin synthesized hundreds of tryptamines and phenethylamines (Shulgin & Shulgin, 1991, 1997). Dr. Shulgin predicted that by the year 2060, over a thousand similar hallucinogens would be discovered (Biello, 2008). A reason to highlight these potential findings is the therapeutic qualities of some hallucinogens.

The Multidisciplinary Association for Psychedelic Studies (MAPS) has been conducting research for many years into the use of certain hallucinogens among humans in the search for cures for many mental and physical health conditions. A visit to their Web site indicates a variety of lines of inquiry. For instance, researchers have been involved in studies examining the utility of MDMA, or ecstasy, to treat patients suffering from post-traumatic stress disorder; the drug could also be used to relieve anxiety and pain in end-stage cancer patients

(Check, 2004; Sessa, 2005). Researchers are also examining the use of psilocybin and LSD to alleviate cluster headaches (Sewell et al., 2006). Other researchers have examined the use of psilocybin to achieve spiritual significance and personal meaning (Griffiths et al., 2006). Ketamine has been used to treat chronic pain associated with Reflex Sympathetic Dystrophy (see Harbut & Correll, 2002).

An additional utility of some hallucinogens is their potential for treatment of drug and alcohol addiction. Ibogaine—a very powerful hallucinogen—is one such drug. Ibogaine is illegal in the United States, though legal in many other countries, and dozens of clinics worldwide have used ibogaine in the treatment of addiction (Vastag, 2005). Ketamine, as well, has been used effectively in the treatment of heroin addiction (Krupitsky et al., 2002). Many findings on the medicinal qualities of hallucinogens have emerged in the early 2000s, and the potential therapeutic utility of those, which are yet unexplored, is promising.

SUMMARY

Hallucinogens include a variety of psychoactive substances that produce audio, visual, and temporal distortions commonly referred to as hallucinations. Hundreds of substances have hallucinogenic properties, though common and relatively unique hallucinogens discussed here can be broken down into three general categories: tryptamines (LSD, psilocybin, DMT), phenethylamines (mescaline, MDMA, 2C-B) and dissociative anesthetics (phencyclidine (PCP), ketamine). Hallucinogens were once popular within hippie culture in the 1960s and 1970s, and enjoyed a renaissance within rave/club culture from the 1990s into the new millennium. Many hallucinogens are illegal to use or possess, though others are not. Some hallucinogens also have medicinal qualities that have been proven to be effective remedies for a variety of ailments affecting physical and mental health.

See also **Ayahuasca; Complications: Mental Disorders; Hallucinogenic Plants; Ibogaine; Plants, Drugs From.**

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BILL SANDERS

HARM REDUCTION. Between the mid-1980s and the early 2000s, harm reduction emerged as a third alternative to the stark choice between legalization and a strict law enforcement oriented prohibition. It is not the only such alternative. Among others, Reuter (1992) suggests pragmatic and compassionate prohibition as an "owlish" alternative to prohibition hawks and legalizing doves. Nevertheless, harm reduction is arguably the most prominent alternative, particularly in the developed world outside the United States.

DIFFERENT DEFINITIONS OF HARM REDUCTION

The term *harm reduction* is highly controversial, particularly in the United States, in part because it is variously defined by different people. For example, MacCoun (1998) distinguishes between micro- and macro-harm reduction by using the following simple equation: The total drug-related harm equals the amount of drug use multiplied by the average harm per unit of drug use.

The goal to reduce total drug-related harm, what MacCoun terms "macro- harm reduction," is not particularly controversial, but there are broadly speaking two schools of thought concerning how best to achieve this end. One school, which might be termed *use reduction*, argues that the surest way to reduce drug-related harm is to reduce drug use.

The second school advocates reducing total harm by making drugs less harmful, that is, by reducing the average harm per unit of drug use. In MacCoun's terms, this is "micro- harm reduction," or what is more commonly called simply *harm reduction*. This school of thought questions

aggressive efforts to reduce drug use because they can increase the average harm per unit of drug use so much that total harm goes up, even if drug use is reduced. For example, restricting syringes might have a modest effect on injection drug use yet greatly increase the frequency of needle sharing and, hence, transmission of blood-borne diseases, including HIV/AIDS and Hepatitis C.

Just as some harm reduction advocates fear that suppressing drug use might increase harm per unit of drug use, some use reduction advocates fear that reducing drug harmfulness might increase the amount of drug use. This second effect could occur because of *risk compensation*: Reducing the costs of an activity can increase the likelihood and frequency of participation, whether the costs reduced are direct dollar costs (economists such as Grossman [2004] have shown convincingly that drug use goes up when drug prices go down) or non-dollar costs such as health risks. This second effect could also occur if government funding of harm reduction programs was misunderstood as tacitly condoning drug use.

PROBLEMS WITH EVALUATING PROGRAMS AND POLICIES

In principle, programs or policies targeted at either term on the right hand side of the equation above (amount of drug use or average harm per use) have potential to either reduce or increase total drug-related harm. So the merits of a program or policy are hard to establish deductively. But in theory one could simply measure or estimate whether a program or policy had a greater effect in the intended direction on the targeted term or a greater unintended adverse effect on the other term in the equation. In practice, data and other limitations interfere, so researchers can make only rough estimates of the magnitude of intended effects and sometimes almost no reliable quantitative estimates of unintended side-effects.

Opiate Substitution Therapies. Perhaps the strongest evidence in support of such programs and policies come from opiate substitution therapies (OST). When people who are dependent on heroin receive treatment that includes an opiate agonist, substantial improvements in health, social, and criminal justice outcomes often follow. Some opiate agonists, such as the methadone, are not particularly controversial among use reduction advocates. Indeed, methadone maintenance was traditionally seen as a form of drug treatment, not a harm reduction program.

Three factors complicated this view. The first was the advent of HIV/AIDS in the 1980s. Whereas historically it was common to try to gradually reduce the methadone dose over time to get a patient drug-free, high relapse rates and the great risk that relapsing injectors would become HIV-infected encouraged a shift toward viewing indefinite maintenance on methadone as a successful outcome. Second, there has been a more general conceptualization of drug dependence as a chronic relapsing condition that should be managed indefinitely, akin to asthma, not as something to be *cured* by emphasizing abstinence. Third, evidence has accumulated from Switzerland and elsewhere that medically supervised legal heroin prescription produces improved outcomes not altogether different than those offered by methadone maintenance. Some claim that recruitment and retention into such heroin maintenance programs can exceed that achieved with methadone maintenance.

As of 2008, in countries where use reduction policy dominates, methadone maintenance is generally accepted as a legitimate form of drug treatment, whereas heroin maintenance is dismissed as an irresponsible form of harm reduction. Among those advocating harm reduction there is generally more openness toward heroin maintenance, although implementation is still not widespread.

Syringe Exchange Programs. Among harm reduction programs, the second largest body of evidence concerns syringe exchange programs (SEP). The conventional wisdom among scholars who study drug policy is that SEP is effective at reducing the spread of HIV without increasing rates of injection drug use among existing users. SEP are not as effective at controlling the spread of Hepatitis C (which is more virulent), but these programs can have the important side benefit of bringing injection drug users into regular contact with service providers who can offer treatment referrals and other support services.

Supervised Injection Facilities. The third largest body of literature concerns supervised injection facilities (SIFs). The most common form of acute

drug-related mortality is heroin overdose. Heroin overdose is readily treatable if detected early enough, so harm reduction advocates suggest allowing heroin users to inject in a supervised facility where there is a staff member who can contact emergency medical personnel promptly if there is a problem.

DRUG TESTING, EDUCATION, AND LOCAL CODES

Another type of harm reduction is offering free testing of drugs. Particularly for some so-called club drugs such as ecstasy, adverse reactions are often caused by an adulterant (e.g., amphetamine), not by the drug that the user intended to consume. Informal drug testing services provided by the user community itself were not uncommon in the U.S. in the 1970s, but more formal versions have emerged in Australia and several European countries over the last ten years (MacCoun, 2007).

Education about responsible or safe drug use is another form of harm reduction. A classic example concerns drug use at all night dance parties, or raves, where drug-related dehydration and hyperthermia are important and sometimes fatal risks, but ones that can easily be countered by drinking plenty of water and taking breaks.

Those same risks can be countered not only via user education but also via municipal code enforcement. Some night clubs eliminate cold water taps in bathrooms to encourage patrons to buy alcoholic drinks, but that practice can be banned, with the ban enforced in the same way that fire codes and other public health codes are enforced by threatening to close the establishment or revoke its liquor license.

U.S. VERSUS INTERNATIONAL VIEWS ON HARM REDUCTION

There are many drug-related harms, and harm reduction efforts as of 2008 have primarily focused on only a subset, notably (1) transmission of blood-borne diseases via injection drug use, (2) heroin overdose, and (3) harms associated with club drugs. Perhaps not coincidentally, those harms account for a substantial share of all drug-related harms in Australia and many European countries, which are seen as leaders in harm reduction. However, in the United States, roughly three-fourths of drug-related harms are associated with cocaine (including crack) and methamphetamine and are often connected to drug-related crime and drug markets, not directly to drug use per se.

Perhaps harm reduction is viewed more skeptically in the United States because it less relevant to most of the U.S. drug problem, or perhaps harm reduction is less relevant for the bulk of U.S. drug problems because international leaders of the harm reduction movement have focused on inventing ways of dealing with the issues that are of greatest concern in those countries.

If the United States were to adopt a harm reduction philosophy that focused on drug-related crime and market violence, the resulting policies might look very different than those typically associated with the harm reduction movement. In particular, currently police often play a passive role in harm reduction. For example, they may not arrest injection drug users for possessing a syringe, and as a result, those users are less likely to need to borrow a syringe when they next inject themselves. However, if the harm reduction objective is reducing drug market–related violence, police may need to play a more active role. Indeed, interventions such as Boston's Operation Ceasefire that dramatically reduced drug-related homicide among youthful drug sellers (Braga et al., 2001) can be seen as successful harm reduction interventions. These programs greatly reduce drug-related homicides without specifically trying to reduce drug use. However, they are rarely conceptualized or discussed as such because the term "harm reduction" is so controversial in the United States.

Some of the controversy regarding harm reduction may derive unfortunately from its association for some people with legalization. While certainly many people who support legalization also support harm reduction, it may not be true that most people who support harm reduction also support legalization. Then, too, some controversy may derive from a generalized belief that drug use is bad. Harm reduction replaces such an inclusive and simplistic position with one that is more nuanced (e.g., drug use may be bad, but HIV/AIDS is worse, so we will focus on the latter) in the hopes of achieving certain pragmatic outcomes.

Graduated enforcement of prohibitions with particular attention to activities that are seen as most harmful has been accepted in some societies for certain vices: Prostitution in the early 2000s

and gambling in former times might be examples in the United States. Whether harm reduction is good policy toward drugs in a particular jurisdiction depends on the values and preferences of local voters and on program effectiveness. The public needs to examine how much a harm reduction approach may reduce harmfulness and what if any adverse consequences exist for drug use. Neither is easily measured. People may continue to debate harm reduction proposals, but one can hope that the debate will be based on reasoned rather than false arguments.

See also **Drug Testing Methods and Clinical Interpretations of Test Results; Legal Regulation of Drugs and Alcohol; Legalization vs. Prohibition of Drugs: Historical Perspective; Legalization vs. Prohibition of Drugs: Policy Analysis; Methadone Maintenance Programs; Needle and Syringe Exchanges and HIV/AIDS.**

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JONATHAN P. CAULKINS

HARRISON NARCOTICS ACT OF 1914.

The first international drug-control initiative, the 1909 Shanghai Opium Commission, brought the international community together in an effort to curb the illicit traffic and consumption of the narcotic drug opium. The Commission met at conferences at the Hague, Netherlands in 1911 and 1913 and encouraged participants to enact national legislation that would address the narcotics problem in their own countries. During this period the U.S. Congress became aware of the public opinion favoring prohibition of all *moral evils*, especially alcohol and drugs. New York Representative Francis B. Harrison was motivated by both the Shanghai Commission directive to curb narcotics and by the reformists in the Progressive movement in the United States who wanted to eradicate drug use. He proposed two measures: (1) prohibit the importation and nonmedical use of opium and (2) regulate the production of opium in the United States.

Congress enacted the Harrison Narcotics Act in December 1914 with minimal debate because of the general public opinion about drugs.

PROVISIONS OF THE HARRISON NARCOTICS ACT

Congress regulated narcotic drugs by imposing licensing requirements on manufacturers, distributors, sellers, importers, producers, compounders, and dispensers. The Harrison Act required that these parties register with the director of the Internal Revenue Service within the Treasury Department and that they pay a gradually increasing occupational tax. Congress wanted to monitor the flow of opium and coca leaves so that government authorities would have records of any transaction involving these drugs. The drugs were allowed only for limited medical and scientific purposes. Those individuals found in violation of the act faced a maximum penalty of five years in jail, a $2,000 fine, or both.

TREASURY DEPARTMENT REGULATIONS

The Harrison Act was intended to generate revenue by imposing taxes on parties involved in the trade, sale, and distribution of drugs. As a result, Congress entrusted the Treasury Department with enforcement responsibility, in particular the Internal Revenue Service and subsequently the Narcotics Unit of the Bureau of Prohibition. The Treasury Department attempted to limit narcotics to medical and scientific use and prevent their illegal diversion by physicians and druggists. The Harrison Act required pharmacists to review prescriptions to determine if they were a suspicious or coerced prescription (i.e., unusually large quantity).

Sales and transfers of narcotics could only be made through official order forms obtained from the director of the IRS. District offices of the IRS maintained these records for two years. The act permitted a few notable exceptions to filing these forms. For example, qualified practitioners (physicians, dentists, and veterinarians) could prescribe or dispense narcotics to patients without completing the order forms but were required to maintain records of all the substances distributed. Druggists could also fill lawful prescriptions without completing the forms.

The Treasury Department interpreted the Harrison Act to mean prohibiting drug addicts from obtaining narcotics. Addicts were prohibited from registering and could receive narcotics only through a licensed physician, dentist, or veterinarian. The department regulations also prohibited physicians from maintaining a patient-addict on narcotics, a practice frequently used to help addicts avoid severe withdrawal pain while they were weaned from narcotic dependence. The department interpreted possession of narcotics as prima facie evidence of a Harrison Act violation, and the burden of proof shifted to the suspect, who had to document that the narcotics were obtained legally.

The Treasury Department enforced the Act primarily through warnings. However, the department charged physicians and druggists with conspiracy when authorities arrested an individual who possessed narcotics without a prescription made in good faith, and a connection could be made that proved that the physician or the druggist provided the narcotics.

THE HARRISON ACT AND U.S. DRUG POLICY

According to the Harrison Act, physicians could prescribe opiates in the course of professional practice. The police and judiciary, however, interpreted the law broadly in ways that resulted in the arrest, the prosecution, and imprisonment of some physicians under the new law. Health professionals therefore chose not to work with substance users, providing a stark choice for their patients to either stop their drug use or buy from the thriving illicit market. An unintended effect of the law shifted heroin and cocaine consumption into the illicit market. Until 1914 heroin, cocaine, and opium could be purchased at a pharmacy; after 1914 they could only be bought from the illicit market.

In 1918 a government committee attempted to determine the impact of the Harrison Act. The committee estimated that opium and other narcotic drugs (including cocaine, which Congress had erroneously labeled as a narcotic in 1914) had over a million adherents. The committee concluded that the reasons for the growth in narcotic use were due to lax implementation, and thus it called for more rigorous application. A growth in organized crime made drug smuggling profitable. Another unintended consequence was the virtual eradication of opium smuggling because of its bulk but a rise in heroin smuggling because it was a concentrated form of opiate and therefore less bulky.

In 1924 Congress attempted to further tighten restrictions by banning heroin for medicinal use. It also prohibited doctors from working with addicts. Pharmaceutical morphine supplies, which were unadulterated, began to rapidly dwindle and were replaced by a thriving illicit trade in adulterated heroin.

Many critics of the Harrison Act argue that the legislation created more problems than it solved. In particular, they charge that the measure failed to eradicate the narcotics problem, primarily because it failed to prohibit the sale and distribution of marijuana. In addition detractors argue that the act did not resolve the issue of whether drug addicts should be treated as criminals or as patients requiring medical treatment. They also contend that the courts hampered the Treasury Department's enforcement authority. Specifically, courts prohibited the department from seizing narcotics, interpreting the Act as a means to collect revenue, rather than as a penal measure. After the Harrison Act was passed, illicit use of narcotics increased initially as a result of these omissions or ambiguities.

Despite these criticisms, the Harrison Act is significant because it led to a national focus on the dangers of narcotics and drug abuse. Most important is that the Act served as the impetus for further legislation, such as the 1970 Controlled Substances Act, in the attempt to combat the illegal sale, distribution, and consumption of narcotics and other abusable substances in the United States, while ensuring their availability for medical purposes.

See also **Controlled Substances Act of 1970; Legal Regulation of Drugs and Alcohol; Prohibition of Alcohol.**

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ALAN MINSK
REVISED BY DEAN WHITTINGTON (2009)

HASHISH. Hashish is the Arabic word for a particular form of Cannabis sativa; it came into English at the end of the sixteenth century. Hashish is the resin derived principally from the flowers, bracts, and young leaves of the female hemp plant. The resin contains cannabinoids—the one of major interest being tetrahydrocannabinol (THC). The THC content will vary depending upon the composition of the hashish, but often it is about 4 percent or more. Usually the resinous portion is sticky enough to allow the material to be compressed into a wafer or brick. Some preparations contain only the resin and are known as hashish oil. Similar preparations of the resinous material and flowering tops of the plant have been given a variety of names in different regions—*charas* in India, *esvar* in Turkey, *anascha* in areas of the former USSR, *kif* in Morocco and parts of the Middle East.

One of the ways in which hashish is prepared is to boil *Cannabis* leaves in water to which butter has been added. THC, being extremely fat-soluble, binds with the butter, which can then be used for making various confections, cookies, and sweets; these are eaten to obtain the effects of the drug. Although hashish is often taken by mouth, it can also be smoked, just as marijuana is.

Hashish was introduced to the West in the middle of the nineteenth century by a French psychiatrist, Moreau de Tours, who experimented with the drug as a means of understanding the phenomenon of mental illnesses. He not only experimented on himself but on a coterie of friends of considerable literary talent. These included Théophile Gautier, Alexander Dumas, and Charles Baudelaire. This group named themselves "Le Club des Haschischins" or "The Club of Hashish-Eaters." The lurid descriptions of the drug effects by these talented writers no doubt helped popularize the drug. Most of their accounts dwelt on beautiful hallucinations and a sense of omnipotence. Doses must have been large, since the effects described are more characteristic of hallucinogenic drugs than effects experienced by present-day users (smokers) of marijuana.

Hashish was introduced into England at about the same time, by an Irish physician, William Brooke O'Shaughnessy, who had spent some time in India, where he had become familiar with it. The material was soon hailed as a wonder drug, being used for all sorts of complaints: pain, muscle spasms, convulsions, migraine headaches, and inflamed tonsils. As most of the preparations were weak and the doses used were small, any beneficial effects might be attributable to a placebo effect.

A preparation, Tilden's Extract of Cannabis Indica, became a popular remedy in the United States in the 1850s. An amateur pharmacologist, Fitz Hugh Ludlow, used this preparation for self-experiments in which he was able to explore its hallucinogenic properties. He may have become somewhat dependent on hashish but finally gave it up. His descriptions of the effects of the drug were similar to what had previously been experienced by Asian users: euphoria and uncontrollable laughter; altered perceptions of space, time, vision, and hearing; synesthesias and depersonalization.

Hashish is currently the most potent of all *Cannabis* preparations: A lot of drug effect is packed into a small parcel. Regulation of the dose is difficult because of its variable potency, and labels for street drugs are notoriously unreliable, however. What may be sold as hashish may often be closer to ordinary marijuana in potency.

See also **Amotivational Syndrome; Creativity and Drugs; Epidemics of Drug Abuse in the United States; Plants, Drugs From.**

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LEO E. HOLLISTER

HEMP. In the narrow sense, hemp refers to a fiber derived from certain strains of *Cannabis sativa*, a bushy herb that originated in Asia. In the broader sense, it also denotes the other use of the plant, as a source of marijuana. Although *Cannabis sativa* is generally considered to be a single species, two genetic strains show considerable differences. One is used for fiber production and has been so used for centuries to make rope, floor coverings, and cloth. Hemp plants have been grown for this purpose as commercial crops in Asia and even in colonial America; during World War II, they were grown in the midwestern United States when the Asian supply was unavailable.

The other strain of the hemp plant produces a poor fiber but has a relatively high drug content; it is used for its psychoactive effect. Near the end of the nineteenth century, the Indian Hemp Drug Commission (1895) produced one of the first major assessments of *cannabis* as a drug, finding it not a major health hazard. Consequently, it remains in legal use in India for both medicinal and social purposes, where it is called bhang.

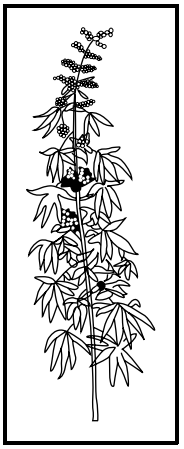

Figure 1. Hemp plant. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Plants, Drugs From.**

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HEPATITIS C INFECTION. In the 1970s it became clear that infection with hepatitis A or B could not explain a large proportion of cases of both acute and chronic hepatitis, and another virus was suspected. This non-A, non-B hepatitis virus was identified in 1989 and designated the hepatitis C virus (HCV). HCV belongs to the flaviviridae family that is distantly related to hepatitis G virus but not to any other known hepatitis viruses. HCV is an RNA virus with a single strand molecule of about 9,500 nucleotides. The enzyme responsible for viral replication lacks the ability to correct copying errors, resulting in the large viral diversity that is characteristic of HCV. This heterogeneity is extremely important because it affects immune response, diagnosis, and response to treatment. Closely related viral strains are called quasispecies and are about 95 percent similar in their RNA sequence. More distantly related strains share only about 80 percent or less of their genetic sequence and are called *genotypes*. Over time HCV virus evolved into six distinct genotypes. The world distribution of these genotypes is approximately as follows: Genotype 1 is most common (60 to 70% of isolates) in the United States and Europe; genotypes 2 and 3 are less common in these areas, while genotypes 4, 5, and 6 are rare. Genotype 2 is present worldwide, and genotype 3 is most common in India, the Far East, and Australia; genotype 4 is most common in Africa and the Middle East; genotype 5 is most common in South Africa; and genotype 6 is most common in Hong Kong, Vietnam, and Australia. The clinical significance of viral genotypes is in their response to interferon-based therapy. The sustained virologic response to therapy by pegylated interferon plus ribavarin ranges from about 40 to 50 percent with genotype 1 (including

1a and 1b) to as high as 70 to 80 percent with genotypes 2 and 3 (Lauer & Walker, 2001).

EPIDEMIOLOGY

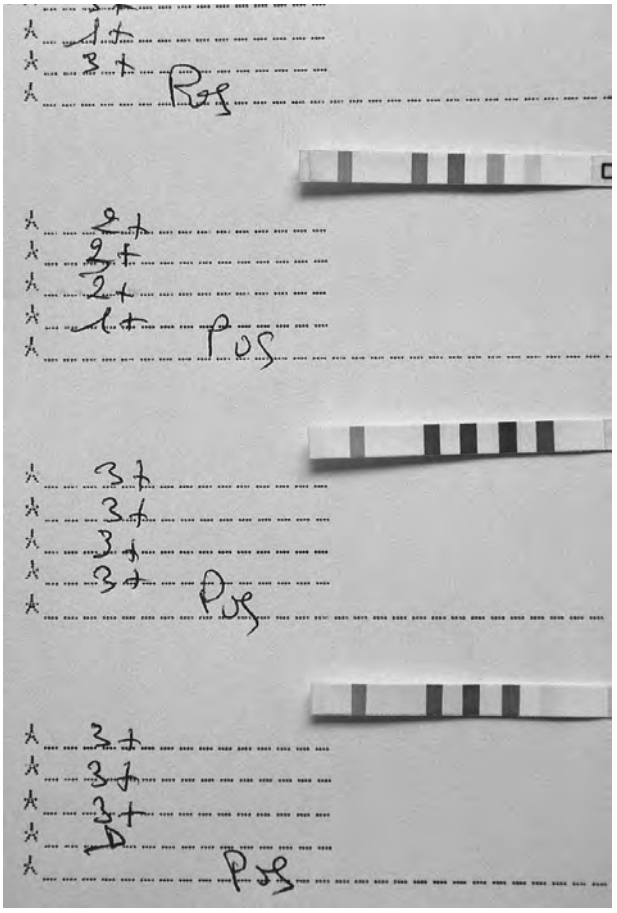
It is estimated that there are about 20,000 new acute cases of HCV infection per year in the United States, a decline from 230,000 cases per year in the 1980s. Most of these cases appear to be related to drug use. Transfusion associated acute HCV infection has been reduced almost to zero in the past 20 years. Chronic HCV infection is the most common chronic liver disease and the majority of liver transplants in the United States are performed for this condition. Additionally, about 8,000 to 13,000 people die each year as a consequence of chronic HCV infection. Approximately 1.6 percent of people in the United States are positive for HCV antibody, or 4.1 million people who are positive for antibody, translating to about 1.3 percent or 3.2 million persons that test positive for HCV virus in their blood. Most cases of acute hepatitis C have no symptoms and only 25 percent are clinically detected. Severe acute hepatitis C cases are rare (Alter & Mast, 1994).

TRANSMISSION AND RISK ODDS

The majority of HCV-infected patients in the United States acquired the disease through intravenous drug use or blood transfusion. However, as of 2008, transfusion-related infection is rare since testing of blood-derived products began in 1990. About 40 percent of patients lack identifiable risk factors for HCV infection but high-risk behavior at some point in their lives often can be detected on careful questioning. About 60 percent of newly acquired infection is attributable to drug use. A variety of behaviors and exposures have been shown to substantially increase the risk of infection with HCV. Intravenous drug use confers an odds ratio of infection of about 50, meaning that individuals who use drugs intravenously have 50 times the risk of HCV infection as individuals who do not inject drugs. Shared needles or other paraphernalia remain the most common route of acute HCV infection in the United States. HCV is also associated with intranasal cocaine use, most likely due to blood on shared snorting devices. Before routine screening of blood-derived products began, blood transfusion carried an odds ratio of about 11. The estimated risk as of 2008 is less than one in a million per unit transfused. Sexual activity with an intravenous drug user results in an odds ratio of about 6. A jail stay of more than three days confers an odds ratio of about 3. Religious scarification (i.e., creating ritual scars on the skin) carries an odds ratio of about 3. Injury by a bloody object or piercing one's ears or other body parts increases the odds ratio to about 2. A history of an immunoglobulin injection carries an odds ratio of 1.6. Other important risk factors include being a healthcare worker, transmission in the context of receiving health care (e.g., while in the hospital), organ transplantation and perinatal transmission (where the risk is about 5% higher if a baby's mother is co-infected with HIV). Sexual contacts with either heterosexual or homosexual partners appear to increase risk for HCV transmission only slightly. The estimated risk is about 0.1 percent a year. However, the risk is higher if partners are co-infected with HIV. Routine household contacts are at no increased risk of transmission. Tattooing, body piercing, and commercial barbering may also transmit HCV on rare occasions (Alter & Mast, 1994).

CLINICAL PRESENTATION AND PROGNOSIS

Acute infection with HCV most often produces no symptoms and rarely results in liver failure. It is responsible for about 20 percent of acute cases of hepatitis in the United States. Less that 25 percent of patients develop jaundice. Other symptoms are non-specific and include malaise, nausea, and right upper abdominal pain. About 80 to 100 percent of acute cases develop chronic presence of the virus in their blood and 60 to 80 percent have abnormal liver enzymes tests. Approximately 15 percent of patients may spontaneously clear the virus early after acute infection, but this is unlikely to occur after the virus has persisted for more than 6 months. Patients with chronic infection often show no symptoms or have non-specific complaints such as fatigue (most frequent), nausea, anorexia, sore muscles or joints, and weight loss. These symptoms often alter the individual's quality of life and may improve after successful treatment of the HCV infection. There is no correlation between symptoms, laboratory abnormalities, or liver biopsy histology, but patients with cirrhosis are more likely to be symptomatic. Interestingly, HCV infection is also associated with cognitive impairment independent of the severity of liver disease.



Hepatitis C virus screening with Western-Blot, or immunoblot assay. Test Serum is incubated on nitrocellulose strips, on which four recombinant viral proteins are blotted. Color changes indicate that antibodies are adhering to the proteins. An immunoblot is considered positive if two or more proteins react and is considered indeterminate if only one positive band is detected. GARO/PHOTO RESEARCHERS, INC.

The natural history of HCV infection is difficult to define both because of the long course and the fact that the disease is not progressive in all patients. Both host and viral factors are responsible for the variability in progression. Factors that appear to hasten disease progression include positive HIV status, alcohol and marijuana use, infection after the age of 40 to 55, obesity, diabetes, and liver steatosis (also known as fatty liver). Some studies suggest that after 10 to 20 years the rate of cirrhosis in patients with chronic HCV infection may be as high as 50 percent, though much lower rates of cirrhosis have also been reported. Survival is probably not affected by HCV infection, but overall mortality increases once cirrhosis develops. The risk of liver decompensation in the setting of cirrhosis is about 3 to 4 percent annually. The most common sign of decompensation is accumulation of ascites (fluid in the abdomen). Once decompensation occurs the likelihood of survival at 5 years is 50 percent. The risk of hepatocellular carcinoma (a cancer of the liver) is about 1 percent per year once cirrhosis develops, so that screening for this complication is recommended every 6 months. (Alter & Mast, 1994).

DIAGNOSIS

The presence of viral RNA in the blood is detectable within days after acute exposure. Serum liver test markers (aminotransferases) become elevated in 6 to 12 weeks after exposure, and an HCV antibody test may become positive as soon as 8 weeks after exposure. Patients with known exposure should also undergo testing.

TREATMENT

The goal of treatment of chronic HCV infection is to achieve viral eradication that improves clinical outcomes. Several small studies suggest that treatment of acute HCV infection may result in rates of sustained virologic response rates in excess of 80 percent, but the optimal regimen and timing of therapy remain to be determined. The majority of treatment trials for acute HCV infection used interferon treatment alone. Successful eradication was predicted by achieving a sustained virologic response, that is, no detectable virus 6 months after treatment is completed. Abstaining from alcohol and maintaining a healthy weight are also part of the management of chronic HCV infection. The treatment of chronic HCV infection as of 2008 consists of combination therapy with pegylated interferon injection administered weekly and daily ribavirin tablets. For reasons discussed below, some patients with chronic HCV infection are not candidates for treatment; others do not agree to be treated, so that less than 20 percent of patients ultimately receive treatment. Further, not all individuals in whom treatment is begun successfully complete a full course (i.e., 48 weeks) of treatment. Sustained virologic response depends on many factors and typically ranges from 40 percent to 80 percent depending on the viral genotype and the patient's pretreatment characteristics. Typical patients for whom therapy is widely

accepted are older than 18 years of age and have an abnormal alanineaminotransferase (a liver enzyme) level and a liver biopsy showing significant fibrosis with compensated liver disease. Although the decision to undergo treatment has to be individualized, persons with uncontrolled major depression, autoimmune hepatitis, untreated hyperthyroidism, or who are recipients of a renal, heart, or lung transplant should not be treated. This is also true for those who are pregnant or unwilling to practice adequate contraception (Seef & Hoofnagle, 2002; Hoofnagle & Seef, 2006).

See also **Complications; Injecting Drug Users and HIV.**

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PETR PROTIVA

HEROIN. Morphine was first identified as the pain-relieving active ingredient in opium in 1806. But morphine was not free of the habit-forming and toxic effects of opium. By the late nineteenth century, the idea of modifying molecules to change their pharmacological actions was well established. It seemed quite reasonable to use this approach to develop new chemical entities that might be free of the problems seen with morphine. In Germany, in 1898, H. Dresser introduced such a new drug—3,6-diacetylmorphine—into medical use; it was named there by the Bayer Company, which produced and marketed it, named it heroin (presumably from *heroisch*, meaning "heroical"), because it was more potent than morphine.

Although heroin is structurally very similar to morphine, it was hoped that it would relieve pain without the tendency to produce addiction. Turn-of-the-century medical writings and advertisements, both in Europe and the United States, claimed that heroin was effective for treating pain and cough. Many suggested that it was less toxic than morphine and was nonaddictive. A few even suggested that heroin could be a nonaddicting cure for the morphine habit. Clearly, this was not the case, and within a year or two of its introduction, most of the medical community knew so. By the 1920s, heroin had become the most widely abused of the opiates.

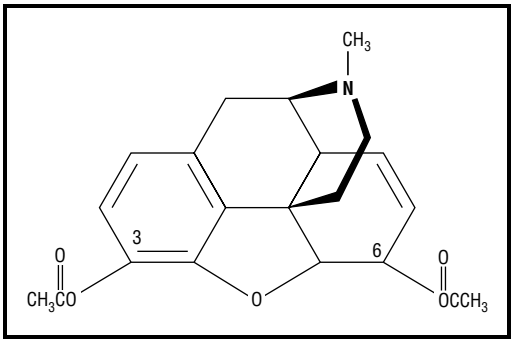

Figure 1. Chemical structure of heroin. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

PHARMACOLOGY

Heroin is a white powder that is readily soluble in water. The introduction of just two esters onto the morphine molecule changes the physical properties of the substance such that there is a significant increase in solubility, permitting solutions with increased drug concentrations. A more subtle advantage of heroin is its greater potency compared to morphine. The volume of drug injected may be particularly important when high doses are used. Thus, 1 gram of heroin will produce the effects of 2 to 3 grams of morphine; by converting morphine to heroin, producers increase both the potency and the value of the drug.

Following injection, heroin is very potent, with the ability to cross the blood-brain barrier and enter the brain. This barrier results from a unique arrangement of cells around blood vessels within the brain, which limits the free movement of compounds. Many factors contribute to the barrier—in general, the less polar a drug, the more rapidly it enters the brain. Heroin, however, has a very short half-life in the blood (amount of time that half the

drug remains). It is rapidly degraded by esterases, the enzymes that break ester bonds. The acetyl group at the 3-position of the molecule is far more sensitive to these enzymes than the acetyl group at the 6-position. Indeed, the 3-acetyl group is attacked almost immediately after injection and, within several minutes, virtually all the heroin is converted to a metabolite, 6-acetylmorphine. The remaining acetyl group at the 6-position is also lost, but at a slower rate. Loss of both acetyl groups generates morphine. It is believed that a combination of 6-acetylmorphine and morphine is responsible for the actions of heroin.

MEDICINAL USE

The pharmacology of heroin is virtually identical to that of morphine. This probably reflects its rapid conversion to 6-acetylmorphine and morphine. Detailed studies comparing the actions of heroin and morphine in cancer patients with severe pain have shown very little difference between the two agents, other than simple potency. Heroin may have a slightly more rapid onset of action than morphine and it is certainly two to three times as potent (presumably due to its greater facility in crossing the blood-brain barrier). This difference in potency is lost with oral administration. The pain relief (analgesia) from both agents is comparable when the doses are adjusted appropriately. At equally effective analgesic doses, even the euphoria seen with heroin is virtually identical to that of morphine. From the clinical point of view, there is little difference between one drug and the other. Both are effective analgesics and can be used beneficially in the treatment of severe pain. Heroin is more soluble, which makes it somewhat easier to give large doses by injection, with smaller volumes needed. Many of the similar semisynthetic agents, such as hydromorphone, however, are many times more potent than heroin and offer even greater advantages.

One widespread use of heroin in the United Kingdom was in the early formulations of Brompton's Cocktail, a mixture of drugs designed to relieve severe pain in terminal cancer patients. The heroin employed in the original formula is now typically replaced with morphine without any loss in effectiveness. For many years, some groups have maintained that heroin is more effective in the relief of cancer pain than morphine is. Careful clinical studies show that this is not true, but the most important issue is using an appropriate dose. Thus, heroin offers no major advantage over morphine from the medical perspective.

STREET HEROIN

Since heroin has no approved medical indications in the United States, it is only available and used illicitly. The marked variability of its purity and the use of a wide variety of other substances and drugs to "cut" street heroin poses a major problem. This inability to know what is included in each drug sale makes the street drug more than doubly dangerous. Typically, heroin is administered intravenously, which provides a rapid "rush," a euphoria, which is thought to be the important component of heroin's addictive properties. It can be injected under the skin (subcutaneously, SC) or deep into the muscle (intramuscularly, IM). Multiple intravenous injections leave marks, called tracks, in a much-used injection site, which often indicate that a person is abusing drugs; but heroin can also be heated and the vapors inhaled through a straw (called "chasing the dragon"). It can also be smoked in a cigarette. While the heat tends to destroy some of the drug, if the preparation is pure enough, a sufficient amount can be inhaled to produce the typical opiate effect.

Heroin use is associated with tolerance and dependence. Chronic use of the drug leads to a decreased sensitivity toward its euphoric and analgesic actions, as well as to dependence. Like morphine, the duration of action of heroin is approximately 4 to 6 hours. Thus, addicts must take the drug several times a day to prevent the appearance of withdrawal signs. Many believe that the need to continue taking the drug to avoid withdrawal enhances its addictive potential.

Patients taking opiates medicinally can be taken off them gradually, without problems. Lowering the opiate dose by 20 to 25 percent daily for two or three days will prevent severe withdrawal discomfort and still permit rapid taper off the drug. Abrupt withdrawal of all of the drug is very different—and leads to a well-defined abstinence syndrome that is very similar for both heroin and morphine. It includes eye tearing, yawning, and sweating after about eight to twelve hours past the last dose. As time goes on, people develop

restlessness, dilated pupils, irritability, diarrhea, abdominal cramps, and periodic waves of gooseflesh. The term *cold turkey* is now used to describe abrupt withdrawal with the associated gooseflesh. The heroin withdrawal syndrome peaks between two and three days after stopping the drug, and symptoms usually disappear within seven to ten days, although some low-level symptoms may persist for many weeks. Babies of mothers dependent on opiates are born dependent, and special care must be taken to help them withdraw during their first weeks. Medically, although miserable, heroin withdrawal is seldom life threatening—unlike withdrawal from alcohol, which can sometimes be fatal.

OVERDOSE

Overdosing is a common problem among heroin addicts. The reason is not always clear, but wide variation in the purity of the street drug can make it difficult for the addict to judge a dose. Some impurities used to cut the drug may be toxic themselves. With overdose, a person becomes stuporous and difficult to arouse. Pupils are typically small and the skin may be cold and clammy. Seizures may occur, particularly in children or babies. Breathing becomes slow, and cyanosis—seen as a darkening of the lips to a bluish color—may develop, indicating inadequate levels of oxygen in the blood. With respiratory depression, blood pressure may then fall. These last two signs are serious, since most people who die from overdose, die from respiratory failure. Complicating the problem is the fact that many addicts may have taken other drugs, used alcohol, and so on. Some of them may have been taken on purpose, and some may have been a part of the street drug.

Naloxone can readily reverse some opiate problems, since it is a potent opiate antagonist. This drug binds to opiate receptors and can reverse morphine and heroin actions. The appropriate dose may be a problem, however, since naloxone can also precipitate a severe abstinence syndrome in a dependent person.

See also **Addiction: Concepts and Definitions; International Drug Supply Systems; Methadone Maintenance Programs; Opioid Complications and Withdrawal; Treatment: A History of Treatment in the United States.**

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HIGH SCHOOL SENIOR SURVEY.

See **Monitoring the Future.**

HISPANIC AMERICANS, ALCOHOL AND DRUG USE AMONG.

Hispanic Americans are a large, growing, diverse group. More precisely, revised U.S. Census Bureau figures released in May 2006 put the total at 44.3 million—of these, 64 percent are Mexican in origin, 9 percent Puerto Rican in origin, and 3 percent Cuban in origin. Yet another 24 percent are classified by the U.S. Bureau of the Census as "other Hispanic," 55 percent of which are from the various Central and South American countries. The rapid growth of the Latino population within the United States also is noteworthy: This population grew by 57.9 percent between 1990 and 2000. A high birth rate and continuous new immigration fuel this growth. The terms *Hispanic* and *Latino* are used interchangeably. Hispanic is commonly used in official statistics, and Latino is more widely used within the population itself.

On average, Hispanics are younger than other minorities and other American population groups. When youthfulness is combined with poverty or discriminatory practices, the result sometimes is a

disproportionate degree of conflict with law enforcement, especially in connection with drug abuse and drug dealing. The media coverage of these conflicts may lead to prejudicial beliefs about Latinos and drug use.

Most Hispanic Americans live in urban areas of the United States. Lacking other options, they are steadily crowding into the poorest sections of New York, Los Angeles, Chicago, and other large cities. In 1999, 22.6 percent of Latinos in the United States lived in poverty compared with 24.9 percent of black families and 12.4 percent of all other Americans. Poor education, difficulty with the English language, and urban concentration can compound this impoverishment—as it has for the other immigrant minorities in the United States—thereby contributing to the complexity of modern urban problems that they must face daily.

All segments of this highly diverse group are changing rapidly. From 1999 to 2003, Mexican immigration accounted for one-third of the overall flow of more than 1 million immigrants to the United States per year, and these numbers are rising. The foreign-born population is expected to grow, until by 2050, it is estimated that nearly 25 percent of the U.S. population will be of Hispanic origin. Many of the newcomers crowd into old *barrios* (neighborhoods), and this reduces the quality of life for older residents. Great pressure is therefore exerted on local educational services, health resources, job sources, and job-training services—a pressure that is compounded by problems of acculturation.

Many Mexican-American communities predate the Mexican-American War of the 1840s, but other Latino communities have become established in significant numbers only since World War II. Puerto Ricans, for example, settled mostly in the large cities of the Rust Belt (or Manufacturing Belt formed by parts of the Northeast, Mid-Atlantic, and Upper Midwest states) in the late 1940s and early 1950s, forming a particularly large concentration in New York City. Like Mexican Americans (Chicanos), they have been sharply affected by shifts in the American economy that relegate poorly educated workers to lower paid service jobs. Central and South Americans are found in diverse locations, with concentrations in New York, Houston, and Los Angeles, where they tend to work at the bottom of the labor market. Cubans, who are concentrated primarily in Miami, have been helped both by a vigorous enclave economy (with Cubans owning many of the enterprises and hiring fellow Cubans) and by Miami's emergence as a center for Latin American trade.

HISPANICS AND ILLICIT DRUGS

Latinos often are typecast as drug users. Such stereotypes persist partly because there is little research information. National statistics about Hispanics mask important variations within the population, not only in ethnicity but also in class and culture. Drug problems of the community are treated principally as criminal phenomena, and indeed, in many states a disproportionate number of Latinos are imprisoned for drug-related offenses. The context for drug use is little studied.

What then is really known about drug use by Hispanics? Specifically, the 2007 National Survey on Drug Use and Health (NSDUH) report showed that Hispanics are generally less likely to use any illicit drug than either blacks or whites. The same survey reported illicit drug use among Hispanics at 6.9 percent (Substance Abuse and Mental Health Services Administration, 2007). Hispanics are most likely to use cocaine, and next most likely (after blacks) to use crack cocaine.

While heroin has posed problems for Latinos, particularly in New York and the Southwest, the prevalence rates for this drug are low. The general population had 136,000 current heroin users in 2005, a figure that rose to 338,000 in 2006 (SAMHSA). Heroin use has been studied in several southwestern communities, in particular in the context of peer group and family in Los Angeles barrios.

The aggregate figures also conceal significant subgroup and geographic differences. Puerto Ricans are especially likely to use cocaine, for example, and Cubans are notably less likely to use any drug. (However, clinical data indicate that Cuban drug use is actually higher than survey data show.) Studies of persons arrested for crimes, for example, show that more than two-thirds of Hispanic arrestees in Chicago, New York, Philadelphia, and San Diego were using drugs, but proportions were far lower in most other cities (U.S. Department of Justice, 1991). More than two-thirds of local jail inmates (68%) were dependent on or abusing drugs or alcohol, according to a 2002 survey of men and

women held in local jails. While 78 percent of white inmates and 64 percent of black inmates were reportedly dependent on or abusing drugs and alcohol, only 59 percent of Hispanic inmates were dependent on or abusing drugs or alcohol (U.S. Department of Justice, 2002).

Differences in drug use by males and females are sharper for Hispanics than for other ethnic or cultural groups. Mexican American and Puerto Rican boys and girls are socialized very differently to alcohol and drug use—that is, there is more parental and community disapproval for girls and more permissiveness for boys. Research also shows that most female heroin addicts usually begin to use the drug with a male friend, spouse, or common-law partner, thus suggesting that the use depends on a relationship. Hispanic women appear to be greatly influenced by traditional ideas about the role of women, even under the pressures of urbanization, acculturation, and poverty (Moore, 1990).

As to adolescents, the most susceptible group, there is little information about how adolescent Hispanic groups differ from other adolescent groups in drug use. National surveys of high school seniors discover only small differences, but the surveys omit dropouts, who are often the adolescents most at risk, and Hispanic adolescents have very high dropout rates. Most studies confirm that the same risk factors that are important for other youth are important for Hispanics: above all, a disruptive family environment, availability of drugs, peer influences, and patterns of unconventional behavior (such as low school achievement, rebelliousness, and early sexual activity). These influences (plus the degree of acculturation and individual judgments of the adolescent) seem to be related, in a general way, with beginning drug use and a steady use of drugs (Booth, Castro, & Anglin, 1990).

One recent study indicated that acculturated Hispanics show patterns of substance abuse that are similar to non-Hispanic whites. "The study showed that 6.4 percent of whites reported using illicit drugs in the previous month, compared to 7.2 percent of acculturated Hispanics. However, less than 1 percent of non–acculturated, Spanish-speaking Hispanics reported use in the same time period" (Medical News Today, 2007). The authors of the study explained that, in states such as California, large Hispanic enclaves have a protective effect on new arrivals that mitigates drug experimentation.

A special factor that affects Latinos is the overriding importance in the culture of the family. This influence has both positive and negative effects. The extended family among Puerto Ricans in New York may limit drug use by protecting and controlling youngsters in both single and two-parent households (Fitzpatrick, 1990). In Cuban families, by contrast, illicit drug use may occur when the family structure is severely disrupted, often by the trauma of refugee migration, and researchers argue that the very cohesiveness of the Cuban family may be associated with parental overprotectiveness and adolescent rebellion, sometimes accompanied by drug use as a symptom (Rio et al., 1990).

Research suggests that Hispanic clients achieve only mixed success in treatment, but that finding needs qualification, due to the limitations of available treatment programs. Because of poverty and residence in blighted areas, a disproportionate number of Latino heroin users, for example, are enrolled in programs that simply administer blocking drugs (e.g., methadone) with virtually no other treatment. Urban drug treatment programs generally face chronic shortages of money and personnel. When drug abusers gain access to broader treatment, failure can often be blamed upon the absence of culturally sensitive therapies (Rio et al., 1990). Fitzpatrick (1990) has suggested that Puerto Ricans in New York City show an "extraordinary" ability to cope with a community saturated with drugs and that efforts should be made to build on this ability.

HISPANICS AND ALCOHOL

Among Hispanic and many other groups, alcohol use has been easier to study than the use of illicit drugs; many of its patterns are similar to and may shed light on drug use. As they do with drugs, Hispanics use less alcohol over their lifetimes than do Anglos (i.e., non-Hispanic white U.S. inhabitants in general, not just those of English ancestry), and their usage is only very slightly more than that of blacks. Again as with drugs, sharp gender differences occur in alcohol use, which are especially noteworthy among immigrants. Among Mexican Americans, the gap between male and female drinking narrows but never disappears in succeeding generations, and much recent research focuses on this acculturation effect, so critical in a large

new immigrant population (Canino, 1994). Among younger women, the narrowing gap seems to reflect both acculturation and upward social mobility. Even within one city, Mexican-American drinking habits vary greatly by class (Trotter, 1985). However, Gilbert found that Mexican Americans in California also identify family, financial, and job problems as factors in abusive drinking; they tend to recognize alcoholism not as a medical problem but as a failure of will (Gilbert, 1985). Certainly there is no one set of beliefs, behaviors, or norms associated with Latinos and drinking. Lifestyle diversity within Latino subgroups suggests the need for a corresponding diversity of treatment approaches. The failure of such standard treatments as Alcoholics Anonymous among Hispanics in certain areas should be noted.

Finally, as noted before regarding drugs, there are important differences in drinking behavior between subgroups of Hispanics. Pentecostal church groups have had notable success in influencing the drinking behavior of some Puerto Ricans, although some clinicians have expressed the view that Puerto Ricans are reluctant to use treatment services. Cuban drinking patterns are generally moderate: Cultural values of self-control forbid discernible drunkenness for both men and women. Increasing acculturation gradually increases alcohol usage but reduces reliance on minor tranquilizers by Cuban women. Of the little information available on the subject, all stresses the importance of individual ethnic experience.

See also **Alcoholics Anonymous (AA); Cocaine; Coping and Drug Use; Crack; Crime and Drugs; Criminal Justice System, Treatment in the; Dropouts and Substance Use; Families and Drug Use; Heroin; Marijuana (Cannabis); Methadone Maintenance Programs; Mexico; National Survey on Drug Use and Health (NSDUH); Opiates/Opioids; Prisons and Jails, Drug Treatment in; Risk Factors for Substance Use, Abuse, and Dependence: Gender; Risk Factors for Substance Use, Abuse, and Dependence: Race/Ethnicity; U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA).**

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HIV (HUMAN IMMUNODEFICIENCY VIRUS).

See **Alcohol and AIDS; Injecting Drug Users and HIV; Needle and Syringe Exchanges and HIV/AIDS; Prisons and Jails: Drug Use and HIV/AIDS in; Substance Abuse and AIDS.**

HIV RISK ASSESSMENT BATTERY (RAB).

The Risk Assessment Battery (RAB) is a self-administered questionnaire designed for use with substance-using populations. It was developed to provide a rapid (less than 15 minutes) and confidential, non interview method of assessing both needle use practices and sexual activity associated with HIV transmission.

The forty-five questions of the RAB are simply worded and use discrete response categories. Respondents are asked to "check off" the answer that best describes their behavior. There are no open-ended questions, minimizing the need for writing skills. A brief set of instructions is included on the first page of the RAB. However, as with all self-administered questionnaires, it is particularly important to provide the respondent with a proper introduction and explanation of the form, its purpose, and how it is to be completed. A staff member should be available during administration of the test to screen for reading difficulties, answer questions as they arise, and ensure that the form is being filled out properly. Given the very sensitive nature of the information collected, it is also important that individuals administering the RAB address the issue of confidentiality. Although the more private approach of the self-administered questionnaire should reinforce the confidential nature of the assessment, it is very important that respondents understand the confidentiality of their responses will be protected.

There are two global sections within the RAB: 1) drug and alcohol use during the past 30 days, and 2) needle use and sexual behavior during the previous 6 months. Questions have been constructed to provide maximum coverage and sensitivity to potential risk behaviors within these categories. Since self-reports may be expected to provide underestimates of behaviors that are socially unaccepted, items have been assembled that assess a wider range of behaviors associated with HIV infection. Thus, questions ask not only about the behaviors directly responsible for viral transmission such as needle sharing and unprotected sexual activity, but also those associated with such activities (e.g., needle acquisition, shooting gallery attendance, exchange of money or drugs for sex). The inclusion of these items is intended to identify individuals at increased risk of HIV exposure even if transmission behaviors are not directly reported. However, endorsement of these "peripheral behaviors" does not prove that transmission behaviors have actually occurred. For example, an individual who indicates that he or she has visited a shooting gallery on numerous occasions during the assessment interval may not have shared a needle or had unprotected sex even though these behaviors are common in shooting galleries. Instead, these peripheral behaviors may be more readily reported by some respondents despite their reluctance to report primary transmission events such as sharing a syringe or unprotected sexual activity.

Scoring. Sixteen items from the RAB are used in the computation of three scores: a drug-risk score, a sex-risk score, and a total score. These scores are calculated by adding responses to selected items. For individual questions, the values range from zero to a maximum of 4. Higher values for items reflect greater frequency of occurrence for the behavior. The eight-item drug-risk score has a range of 0 to 22. The range of the sex-risk score, comprised of nine items, is 0 to 18. This simple scoring system was designed to capture frequency of engaging in each of the reported risk behaviors. Scores for the various items are not differentially weighted. This scoring strategy serves to guard against underestimates of risk resulting from the tendency to underreport participation in behaviors known to be most likely to transmit the AIDS virus.

As a self-administered questionnaire, the RAB offers an efficient tool for screening individuals who may be at risk for HIV infection. The RAB provides a measure of HIV-risk behaviors, which is broken down into subscales for drug risk and sex risk and combined to yield a measure of total risk. A number of studies conducted by the authors and others suggest that when properly administered, the RAB responses are equivalent to those collected via a personal interview. Test-retest reliability has also been found to be relatively high. Most

importantly, the RAB has demonstrated discriminant validity in differentiating between respondents engaging in different drug-use patterns and predictive validity in identifying seroconverters on the basis of higher-risk scores.

As the AIDS epidemic enters its third decade, it has become increasingly important to have valid, reliable, and cost-effective tools to monitor behaviors associated with the transmission of HIV. It is no longer sufficient to direct prevention resources toward populations at risk in a "shotgun" approach to risk reduction. Such a strategy is costly and inefficient since many individuals within risk groups have instituted safer behaviors. Targeting risk-reduction interventions to specific segments of the population at risk and evaluating their efficacy are necessary components in a well-planned approach to HIV prevention. Measures of risk behavior, such as the RAB, are needed to target and evaluate interventions in a more precise manner.

See also **Alcohol and AIDS; Substance Abuse and AIDS.**

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HOMELESSNESS, HISTORY OF ASSOCIATION WITH ALCOHOL AND DRUGS.

As Robert Frost observed in *The Death of the Hired Man*, "home is the place where, when you have to go there, they have to take you in." Not everyone has that privilege, however. The history of homelessness is the history of the social contexts that create both the necessity of refuge and the specific forms it takes. While data about individuals are clues to the larger processes of displacement, they do not explain them. Debates about whether a third or a half of today's sheltered population suffers with current substance abuse often miss this point. Simply put, substance abuse is a significant, but not pervasive, problem among homeless people. It is concentrated among (but not unique to) single men and those who spend unusually long stretches of time in shelters or who "make the loop" among shelters and other institutions reserved for the ill, the wayward, and the dispossessed. This is hardly surprising. While substance abuse usually came before prolonged homelessness, so did a lifetime of poverty, family disruption, and modest educational achievement and vocational development. This constitutes the bundle of liabilities associated with homelessness. But whereas previous generations of impoverished substance abusers scuffled their way through a variety of makeshift economic and housing arrangements that would have disqualified them as homeless by the twenty-first-century definition, the liabilities of that generation play out in a world grown unforgiving at its economic margins and highly dependent on congregate shelters to contain and measure the fallout.

HISTORY

The word *homeless* has a long and complex use. In its most literal meaning of houseless, it has been employed since the mid-1800s to describe those who sleep outdoors or in various makeshifts or who reside in temporary accommodations such as police-station lodgings of earlier generations or emergency shelters of the present day. Another early meaning of the word is not belonging to a place or with the people who live there. This usage was handed down from the largely rural and small-town society of the nineteenth century, in which the coincidence of family and place provided the basis for community and social order, nurturing traditions of mutual aid and the control of troublesome behavior. To be homeless was to be *unattached*, outside this web of support and control; it was to be without critical resources and, equally important, beyond constructive restraint. Many of the young men and women who moved from farm to city, or those who emigrated from abroad during

the nineteenth and early twentieth centuries, were unattached in this respect. Organizations like the YWCA, the YMCA, and various ethnic mutual-aid societies were invented both to help and superintend them by creating surrogate social ties.

By the 1840s many Americans linked homelessness with habitual drunkenness. In the popular view, habitual drunkards, usually men, drank up their wages and impoverished their families; they lost their jobs and their houses and drove off their wives and children by cruel treatment. They became outcasts and drifters, and their wives entered poorhouses while their children became inmates of orphanages. By the 1890s the same logic served to explain the downward, isolated spiral of opiate and cocaine *fiends* (as they were called) and the unhappy circumstances of their families.

Until the early years of the Great Depression (which began in 1929), habitual drunkenness, in particular, often was cited as a principal cause of homelessness. Even so, after the financial collapse of 1893 and an ensuing five-year depression of unprecedented severity, most thoughtful observers did not believe heavy drinking or habitual drug use caused homelessness in any *direct* manner. Although scholarly studies during the first decades of the 1900s were crude by today's technical standards, their explanations of homelessness were not simple-minded. In fact, they foreshadowed twenty-first-century explanations.

Perhaps most important, pre-Depression students of homelessness noted that the ranks of the dispossessed grew and diminished in close relation to economic conditions. They understood that the profound depressions that haunted the economy long before 1929 caused large numbers of people to lose their grip on security. They noted as well that certain occupations were especially affected by seasonal fluctuations in the demand for labor and by technological change. For example, by the 1920s, agricultural workers, cigar makers, printers, and others had high rates of *structural* unemployment. That is, their jobs had been lost permanently to changes in methods of production and distribution.

These scholars also understood the importance of decisions that employers made about hiring and firing. Workers without families to support and those regarded as the least productive were let go first when the economy soured. Usually these were single young women assumed able to return to their natal families, married women presumed to be working for *pin money* (people who today are known as secondary wage earners), older men, and in particular, single men known to drink heavily. Minority racial and ethnic status also marked people for layoff. Conversely, in times of high demand for labor, employers relaxed their standards for hiring and job performance. In boom times all but the most seriously disabled or the most erratic and disruptive heavy drinkers and drug users could find some kind of work. The ranks of the homeless thus thinned considerably.

Pre-Depression observers also emphasized the impact of working conditions, disability, and the absence of income supports on the creation of homelessness. In an era of dangerous work and widespread chronic disease (especially tuberculosis), large numbers of men, in particular, became substantially disabled, often at a young age. In an era before significant public disability benefits or much in the way of welfare or effective medical treatment, they rapidly became abjectly poor, reduced to begging, eating in soup kitchens, and bedding down in mission shelters or the cheapest, most verminous lodging houses (*flophouses*, as they came to be called).

Some of these men were heavy drinkers, and some were habitual drug users, but these problems often developed in the context of poverty and rootlessness. The miseries and long stretches of boredom endemic to poverty were understood to promote frequent intoxication—even during the Prohibition years (1920–1933), when illicit alcohol could be had by arrangement, as could illicit drugs. Certain *hobo* occupations that demanded rootlessness and brought together large groups of men without families were regarded as corrupting and debilitating. Railroad gangers, cowboys, farm workers, lumberjacks, and sailors, among others, pursued risky occupations and lived in ways that provided both motive and opportunity for dissipation. During the Depression it was widely feared that tens of thousands of homeless young people in the United States would be maimed hopping freights and would learn bad habits on the road that would transform them into lifelong tramps.

Finally, related to their understanding of homelessness as an unwholesome and demoralizing experience, early observers paid a great deal of attention to the milieu of homelessness—the urban areas where homeless people congregated and the constellation of institutions with which they were involved. Commonly called *hobohemias* before the Depression and *skid rows* thereafter, such areas were characterized by a particular way of life and a peculiar set of economic and social resources. They were honeycombed with cheap restaurants, residential hotels and lodging houses, private and eventually public welfare agencies, and formal and informal labor exchanges that offered casual (day) work. Skid row (and the segregated satellites that developed in minority communities) was also a world dominated by single men. Saloons (later bars) and sex workers saturated the area. Some were the sites of a vigorous drug trade.

By the 1940s, winnowed by wartime labor demand, skid row was both repository and refuge, mainly for impoverished single men disabled by age, injury, and/or chronic illness. They survived on private charity, meager public welfare allowances, modest pensions, and undemanding work. However, skid-row denizens were not homeless, and from the 1940s through the 1970s, they were more often described as *unattached* or *disaffiliated*. They were homeless in the broader, social sense. Further, and contrary to the enduring stereotype, the residents of skid row were not usually heavy drinkers or habitual drug users. Although perhaps one-third could be so described and while public intoxication was common and visible, heavy drinking or drug taking was, as today, the exception and not the rule.

With the sustained prosperity of the period between 1941 and 1973 and the simultaneous elaboration of the American welfare state, many observers believed that skid row would wither away. The older men would die off or—helped by federal Old Age Security and later by Medicare/Medicaid, state and federal disability benefits, and subsidized housing—would move to better neighborhoods. Or they would remain on a skid row that would be uplifted and transformed by urban renewal projects and effective rehabilitation programs for heavy drinkers and drug users.

In a limited sense, these optimists were correct. The expansion of the welfare state dramatically improved the economic circumstances of the elderly, who are rare among the early twenty-first-century homeless. Aided by federal funds, some cities bulldozed their skid-row areas, thus causing their bricks and mortar, at least, to disappear. But homelessness did not disappear; instead, it underwent an astonishing and tragic transformation. If literal houselessness is used as the definition and measure of the problem, only the Depression produced the prodigious dispossession that characterizes the early twenty-first century.

As opposed to the domiciled isolation of skid row, something like the houseless poverty of the early twenty-first century was first reported in news magazines and the occasional scholarly publication as early as 1973. But it was not until the early 1980s that a new generation of younger homeless people achieved widespread notice. At first, most observers were struck by the apparently very high rates of mental illness, heavy drinking, and drug use among these new homeless people. Explanations of the problem pointed toward nationwide changes in policies that governed commitment to and retention in mental hospitals and incarceration for public drunkenness and minor drug offenses. During the 1960s and 1970s many states deinstitutionalized both people with mental illness as well as alcoholics and addicts. State hospital patients were discharged in wholesale fashion, and new laws made initial involuntary commitments difficult; they also severely limited the duration of involuntary treatment. Many states also decriminalized public drunkenness, referring inebriates to places where they could sober up rather than housing them in jail for thirty days to six months. Similarly, many minor drug offenders were diverted from jails. During the early 1980s many observers, notably those within the Reagan administration, characterized the resurgence of homelessness as a problem related to mental disorder, excessive drinking, habitual drug use, and the new policies that kept people with such problems from their customary lodgings in state hospitals and county jails. Homelessness was described mainly as a problem in the rehabilitation and control of troubled and troublesome people who were not only houseless but barred from their traditional institutional shelters and estranged from family and friends who might take them in.

EARLY TWENTY-FIRST CENTURY VIEWS

Although not discounting this view entirely, most scholars now find it simplistic and unsupported by

the evidence. Although some popular treatments of the subject continue to claim that perhaps 85 percent of homeless people are substance abusers and/or mentally ill, such huge figures are drawn from old studies that were seriously flawed by two related methodological problems. The first requires little explanation: These studies relied for their estimates on *lifetime* rather than *current* measures of problems. In any group not in treatment or recently discharged, a lifetime measure (a determination of whether a person has ever had a severe mental illness or substance-use disorder) will always produce much higher prevalence rates than a measure of current disorder (customarily defined as present within the previous six months or one year).

The second problem is a matter of how homeless respondents were sampled for these studies and concerns the distinction epidemiologists make between *point prevalence* and *period prevalence*. Point prevalence refers to counts conducted at a single moment in time (a snapshot), whereas period prevalence refers to counts taken over time (a motion picture). Longitudinal (period) counts of homeless people will produce much higher numbers than cross-sectional (point-in-time) enumerations, for many more people are homeless during a year than on a given night. People with problems of substance abuse and mental illness move out of homelessness more slowly, so they will be overrepresented in snapshot studies because they are more likely to be counted. Longitudinal studies during the 1990s demonstrated conclusively that a fairly small group of people with very high rates of disorder (usually single men under forty years old) account for a very large percentage of shelter nights in most cities. Since most studies of homeless populations conducted in the 1980s sampled from shelters on a cross-sectional basis, their estimates of substance abuse and mental illness were correspondingly inflated.

With these caveats in mind, it is probably fair to say that among all homeless adults during the previous year, something like half had a substance-use disorder or a major mental illness, alone or in combination. These rates are substantially higher among single men and significantly lower among adults who are homeless in family groups, most often single women.

Even so, prevalence estimates do not explain the causal relationship between homelessness and substance abuse and mental illness. Clearly, most people with such problems never become homeless. To explain why some do, current scholarship has returned—often unwittingly—to themes first sounded a century ago: the relationship of homelessness to changes in the economy and the nature and supply of housing, to the availability (or coverage) and sufficiency of income supports and medical care, and to the tolerance and support capacity of kin. Heavy drinking, habitual drug use, and mental illness are considered in this larger context. Such problems are understood to be among many risk factors that make it more likely that some people will become homeless repeatedly or remain so for a long time. Moreover, scholars are concerned with how such experience wears people down, introduces or rekindles bad habits or poor health, and makes exits from homelessness less likely or short-lived.

Briefly and simply, early twenty-first-century scholarship suggests the following relationship between homelessness and heavy drinking and habitual drug use. The problem of poverty has worsened considerably since the mid-1970s. Changes in the economy have added high-skill, well-paid technical jobs and low-skill, poorly paid service positions, but these changes have simultaneously produced job losses among semiskilled but highly paid workers, primarily in manufacturing. This process of deindustrialization—the historic passage from a manufacturing to a service economy—has been especially hard on those younger members of the huge baby-boom group (boomers are those born between 1946 and 1964), especially Hispanics and African Americans, who have entered a glutted labor market without the advantage of prolonged higher education or advanced technical training.

At the same time, the 1980s brought startling inflation in rental housing costs and a steep decline in the inflation-adjusted value of federal and state welfare benefits and unemployment insurance. In consequence poor people had an increasingly difficult time forming independent households, and poor families became increasingly hard put to support dependent adult members. Simultaneously, America's most rudimentary housing, the old hotels and lodging houses of skid row and similar areas, was decimated by urban renewal.

Ironically, the unprecedented, sustained economic growth of the 1990s aggravated the problem of homelessness. As the decade wore on, shelter counts rose all over the country. In some part, this was because the general prosperity of the 1990s had little effect in the lowest reaches of the income distribution from which most homeless people come. Cutbacks in federal, state, and local welfare eligibility compounded the problem. Further, rapid economic expansion had a significant inflationary effect on rents. Indeed, for the poorest 20 percent of American households, rents increased faster than incomes between 1995 and 1997. Moreover, the number of units renting for $300 per month (in inflation-adjusted dollars) decreased by 13 percent from 1996 to 1998, resulting in the loss of almost one million such units nationwide. At the same time, the number of households assisted by subsidies from the Department of Housing and Urban Development dropped by 65,000 between 1994 and 1998. In sum, the crisis in affordable housing became worse during the great boom (U.S. Department of Housing and Urban Development, 1999). For a variety of reasons, the supply of affordable housing continued to erode during the first decade of the twenty-first century, whereas the need for it spiked. In 2008 about 8 million low-income households paid more than 50 percent of their income in rent, a figure that increased by a third since 2000 (Locke, Khadduri, & O'Hara, 2007).

CHRONIC HOMELESSNESS AND SUPPORTIVE HOUSING

The most significant change in anti-homelessness policy since the 1990s has been federal emphasis on attending to chronic homelessness. With access to federal resources at stake, states have brought their priorities into line. By government definition, a *chronically homeless* person is someone "with a disabling condition" and a substantial and recent history of continuous or episodic homelessness (Caton, Wilkins, & Anderson, 2007). Roughly 20 percent of the homeless (sheltered) adult population meets these criteria, or about 200,000 people. The *lifetime* prevalence of substance use disorder among the members of this group appears to be very high (Caton, Wilkins, & Anderson, 2007).

The chronic homelessness initiative, as it is known, is controversial for a number of reasons but none more important than its tacit reframing of homelessness as a problem of disability rather than income distribution relative to housing costs. By focusing resources on chronic homelessness, the policy addresses the material basis of homelessness in a limited way by combining federal disability benefits with housing subsidies. Given the inadequacy of unskilled wages to housing costs and the poor coverage and low benefits of American income maintenance programs, it is a stopgap approach dictated by political considerations.

Programs implemented under the initiative rely heavily on *supportive housing*. This combines rehousing efforts with medical and social services. The myriad approaches to supportive housing make generalizations difficult, especially in terms of their effectiveness. The most important distinction among models concerns the role of independent housing. In the most traditional approach—the so-called *staircase* or *continuum of care* model—independent living is preceded by a lengthy period of transitional housing in which homeless people live in supervised, congregate arrangements while they get therapeutic and social support and become *housing ready*. In a more recently developed approach, usually called *housing first*, homeless people are placed immediately in their own residences (often with the service agency as the leaseholder) and get services in their homes or by visiting a program. While there is some evidence that the *housing first* approach is highly effective with people with mental illness (compared to *community-based treatment as usual*), there is far less evidence of its effectiveness with substance abusers or those with multiple problems. Understanding and evaluating these approaches to combining housing with treatment is the most important research problem of the current era. Even so, neither approach can succeed outside experimental conditions in the absence of available, affordable housing.

CONCLUSION

Poor people have been badly squeezed since the early 1970s. As a consequence, perhaps three percent of all American adults, about 5.5 million people, experienced at least one spell of homelessness between the beginning of 1985 and the end of 1990 (Burt, 1996). Some, however, experience frequent and prolonged episodes of homelessness, and it is among these people that rates of heavy drinking and habitual drug use are very high. It is

not simply the case, however, that drinking and taking drugs has caused their homelessness. The problems often associated with such habits may have played an important role in job loss, familial estrangement, or displacement from housing, but this is not a new phenomenon.

Now, though, the absorptive mechanisms of earlier generations have gone awry. Deinstitutionalization has been a factor in this breakdown, mainly because community care never has been equal to the unprecedented need. Nonetheless, more important factors in the creation of widespread houseless poverty among heavy drinkers and habitual drug users have been the disappearance of casual labor, the erosion of public benefits and the capacities of kinship, and the virtual destruction of the tough but viable refuge of skid-row housing. In 1970 impoverished heavy drinkers and habitual drug users could almost always find some port in the storm, often by moving from one decrepit hotel to another, frequently pooling resources to rent a room by the week. Since the 1980s they can no longer do this. Thus they have become a large and highly visible proportion of those who inhabit our public places and persist in our shelters month after month.

See also **Alcohol- and Drug-Free Housing; Alcohol: History of Drinking in the United States; Treatment: A History of Treatment in the United States.**

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HOOKAH. A hookah—also known as a waterpipe, hubble bubble, nargile, argileh, shisha, boory, and goza—is a long-necked device used to smoke tobacco. Hookahs may vary in size, shape, and composition, but they all have four main parts: (1) the head, where the tobacco is placed and indirectly heated, (2) a pipe that connects the bowl to the base and dips into the water in the base, (3) the base, which is partially filled with water, and (4) one or more flexible connecting hoses and mouthpieces from which the smoke is inhaled. To use a hookah, charcoal is placed on perforated foil or another type of screen on top of the tobacco-filled head. The charcoal is then lit, and as the user inhales through the mouthpiece, the tobacco smoke passes through the water in the base of the pipe and passes through the hose to the user.

While the exact origin of hookah smoking is unclear, the use of hookahs to smoke opium, hashish, and tobacco is centuries old. Hookah tobacco smoking in the Middle East declined for most of the twentieth century, but it experienced a resurgence in the 1990s. This resurgence occurred at the same time as the introduction of maassel (also spelled mu'essel or mu'assel, and sometimes referred to as shisha in the U.S.), a tobacco sweetened with honey or molasses that is available in a variety of flavors, including apple, banana, strawberry, chocolate, mint, coffee, rose, and vanilla. Hookah use began to spread globally in the late 20th and early twenty-first centuries. In 2007 the American Lung Association described waterpipes as the "first new tobacco trend of the twenty-first century."

Hookahs are generally used in a group setting, either in a private residence or in a public place. In Middle Eastern and Indian countries, hookahs are widely used in coffee houses, restaurants, and hookah

cafes by individuals from many age groups and social classes. In Europe and the United States, hookah lounges (also called hookah bars or cafes) are growing in popularity, especially in cities and near colleges and universities. In 2006 an estimated two-thirds of U.S. states had hookah lounges, with California, Illinois, New York, Texas, and Virginia having the greatest number. U.S. hookah users are primarily young adults between the ages of 18 and 25, and hookahs are particularly popular among college students. Studies published in 2008 estimated that between 15 and 20 percent of college freshmen have smoked tobacco in a hookah in the past month (Eissenberg, et al., 2008; Grekin & Ayna, 2008).

The increasing popularity of hookah use among young adults in the U.S. can be linked to several factors. Unlike cigarette smoking, hookah smoking is an intermittent, uniquely social activity. Hookah lounges provided an opportunity for socialization similar to that of bars and clubs, but hookah lounges have the added appeal of sometimes being open later hours (until 4:00 a.m. in some instances) and sometimes being open to those who are under 21. (Most hookah lounges require customers be of legal adult age, but some establishments that sell herbal maassel may have a lower minimum age.)

Hookah smoking is relatively inexpensive, which also increases its appeal. Waterpipes and maassel are widely available for purchase on the Internet and in certain retail establishments, such as hookah lounges and Middle Eastern markets. In 2008, online prices for packaged maassel range from $7 to $20 for 250 grams, (enough to fill approximately 20 to 30 hookah heads). Maassel is also sold in single-serve packages, called "shots," for less than $1 each. The cost for the use of a hookah and a bowl of maassel at hookah bars ranges from $5 to $20.

The increasing popularity of hookah smoking in the U.S. can also be attributed to the belief, held by the majority of hookah smokers, that hookah smoking is less harmful than cigarette smoking. The fact that hookah smoke is smoother and less irritating than cigarette smoke may help to perpetuate this belief. Unfortunately, this smoothness, combined with the pleasurable smell and taste of the sweetened, flavored tobacco, may actually encourage a hookah smoker to smoke for a longer period of time and to inhale more deeply. The World Health Organization (2005) estimates that hookah users may inhale as much smoke during one hookah session as a cigarette smoker would inhale consuming one hundred or more cigarettes.

A common misperception is that the water in a hookah filters out the dangerous ingredients of the tobacco smoke. While there is minimal research on the subject, it appears that the water in a hookah may filter out only a small amount of the carbon monoxide, nicotine, tar, and heavy metals found in hookah smoke. For example, Shafagoj, Mohammed, and Hadidi (2002) found that less than five percent of nicotine is filtered out into the water. This nominal reduction of nicotine may be offset by a tendency for the hookah smoker to inhale more deeply or more often to get the desired amount of nicotine. It is estimated that a person who smokes a hookah daily absorbs as much nicotine as someone who smokes ten cigarettes per day, while an occasional hookah smoker (someone who smokes once during a four-day period) absorbs as much nicotine as smoking two cigarettes per day (Neergaard et al., 2007).

This nicotine exposure means that hookah smoking has potentially the same risks of dependence as any other way of using tobacco. However, the risks may be slightly decreased because of the intermittent, recreational nature of hookah use. The limited research on hookah dependence suggests that a transition from social to individual patterns of use, sharing less frequently, or a modification of behavior to accommodate hookah use may be signs of possible dependence. A multidimensional approach to both assessment and treatment of hookah smoking may be necessary to take into account the unique intermittent and social nature of this practice.

Several studies have found that tobacco smoked through a hookah produces more tar than tobacco smoked in a cigarette. However, tobacco smoked through a hookah is heated, not burned, and thus reaches much lower temperatures than in a cigarette. The temperature at which tar is produced may be related to how hazardous and carcinogenic it is. More research is needed to determine the amount and nature of tar produced from hookah smoking, including how this varies by type of tobacco, hookah size and composition, and smoking patterns.

The levels of carbon monoxide (CO) produced and absorbed by hookah smoking may be as high or higher than that of cigarettes. A significant amount of this CO is produced by the combustion of charcoal used to heat the hookah tobacco. CO levels can vary greatly, depending on hookah size (CO levels are higher with smaller hookahs), the type of hose used (CO levels are higher with a plastic hose), the type of charcoal, and the type of tobacco. Hookah smoke also has higher levels of toxic heavy metals—such as arsenic, nickel, and lead—than cigarette smoke. It is unclear whether these metals come from the tobacco, the charcoal, the foil often used as a screen, or the metal coating of the hookah bowl. Another health hazard unique to hookah smoking is the spread of infectious diseases. Sharing a waterpipe can spread tuberculosis and viruses such as herpes and hepatitis. The use of disposable mouthpieces can help reduce this risk.

Many factors make it difficult to assess the specific health consequences directly attributable to hookah smoking, including a lack of studies, differing study methodologies (e.g., smoking machines versus human subjects), the simultaneous use of other tobacco products, and the distinct method of smoking involved in using a hookah (e.g., frequency of puffing, depth of inhalation, length of smoking session). In general, however, the available research indicates that hookah smoking carries many of the same risks as cigarette smoking, including exposure to nicotine and tar, and that it may have some unique risks, such as an increased exposure to carbon monoxide, heavy metals, and infectious diseases.

See also **Tobacco: A History of Tobacco; Tobacco: An International Overview.**

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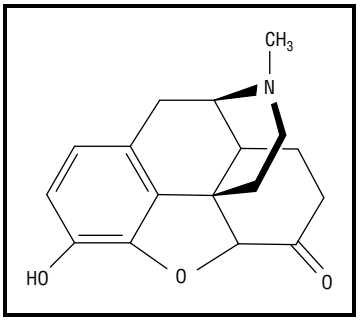

Figure 1. Chemical structure of hydromorphone. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

HYDROMORPHONE. Hydromorphone is a semisynthetic opioid analgesic (painkiller) derived from thebaine, an alkaloid of the opium poppy (*Papaver somniferum*). It is one of the most widely used and effective analgesics for moderate to severe pain and is often referred to as Dilaudid, one of the brand names under which it is sold. Its potency is almost eightfold greater than is morphine's. Structurally, it is quite similar to morphine but most like dihydromorphine, differing only in the replacement of the hydroxyl (–0H) group at the 6-position with a ketone (=0). Thus, it is not surprising that hydromorphone has many of the same side effects—including sedation, constipation, and depression of breathing. Chronic use will produce tolerance and physical dependence, much like morphine. This drug is reported to have high abuse potential, perhaps due, in part, to its very high potency.

See also **Alkaloids; Analgesic; Morphine; Opiates/Opioids; Papaver Somniferum; Tolerance and Physical Dependence.**

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IATROGENIC ADDICTION. Addiction can occur as a side effect of some medical care, and physicians need to understand iatrogenic addiction to weigh the risks and benefits associated with the use of medications such as opioids, benzodiazepines, and stimulants. Not only is the use of these addictive medications a concern, but their underuse is as well, because withholding them from patients out of the fear of causing addiction can result in needless suffering. Physicians are also often reticent to prescribe addictive drugs out of fear of retribution from law enforcement and licensing boards.

DEFINING ADDICTION

There has been confusion surrounding the terminology used to discuss addiction. To help promote uniformity, experts from the American Society of Addiction Medicine, the American Pain Society, and the American Academy of Pain Medicine formed a consensus panel in 2001 to define tolerance, physical dependence, and addiction. According to this panel, *tolerance* can be defined as a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time. *Physical dependence* is defined as a state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood levels of the drug, or administration of an antagonist. It should be noted that tolerance and physical dependence are secondary physical manifestations that can be expected to occur in virtually all patients treated with opioids and benzodiazepines.

In contrast, *addiction* is a primary neurobiological disorder with genetic, psychosocial, and environmental underpinnings. It manifests as behavior, such as impaired control over drug use, compulsive use, continued use despite harm, and craving. It is also characterized by denial, prompting the phrase often heard in addiction treatment settings: "addiction is the only disease that tells you that you don't have it." However, what appears to be addiction is not always addiction. The term *pseudoaddiction* is used to describe behavior that can occur when symptoms such as pain are inadequately controlled. In an attempt to attain relief due to inadequate dosing or increasing symptoms, a patient may repeatedly request more medications or take higher doses than prescribed. What appears to be noncompliance and a loss of control is instead an effort by a suffering patient to bring his symptoms under control. Thus, inadequate dosing in an attempt to avoid addiction can result in behaviors that resemble addiction.

DRUG CONTROL MEASURES

To understand the reticence of many physicians to prescribe addictive medications, it is helpful to review the history of drug control legislation in the United States. In the nineteenth century, few laws in the U.S. governed addictive medications. Opioids and cocaine were ingredients in many patent medications, and physicians freely prescribed them for many medical conditions. Dependence

became a major problem, and—as reported in the October 17, 1903 issue of the Journal of the American Medical Association—physicians were thought to be largely responsible:

> Unfortunately, a large number of cases are reported as directly due to careless prescribing by physicians. Physicians must be guarded and careful in the use of such remedies and must discourage in every possible way the use of proprietary remedies containing them; we must work with all our might for national and local legislation restricting the use of the habit-producing drugs and for the suppression of drug habits. (Drug Habits, 2003)

This perception led to legislation such as the 1906 Pure Food and Drug Act, which required that products containing substances such as opioids and cocaine indicate this on the label. In 1914, the Harrison Narcotics Act was introduced. Though a seemingly reasonable piece of legislation designed to control the nonmedical use of narcotics through taxation and record keeping, the Harrison Act evolved into a drug enforcement instrument that led to the arrest and prosecution of tens of thousands of American physicians over the next 50 years.

The transition of the Harrison Act from a taxation- and documentation-regulatory Act to a drug trafficking control Act can be traced to three Supreme Court cases between 1916 and 1919. In the first, *United States v. Jin Fuey Moy*, 241 U.S. 394 (1916), Dr. Jin Fuey Moy was tried for prescribing 1/16 of an ounce of morphine to a patient who was dependent on opioids. The rationale for prescribing opioids was to prevent the patient from experiencing withdrawal and reduce cravings. This was a common medical treatment strategy at the time, and indeed it is still utilized in methadone and buprenorphine maintenance programs. The Supreme Court decided that the scope of the Harrison Act was limited to taxation and documentation and could not be used for federal control over the practice of medicine. Furthermore, it was the court's decision that the use of the act to suppress the trafficking of opium and other drugs was unconstitutional. As a result of the Court's decision, the Harrison Act could not be used to justify prosecuting physicians such as Dr. Moy.

However, over the next three years, sentiment grew increasingly hostile toward those with an addiction (often referred to as "dope fiends"), as well as the doctors who prescribed opioid medications for them. In 1919, two cases were brought before the Supreme Court to challenge the Harrison Act. In *United States v. Doremus*, 249 U.S. 86 (1919) and *Webb v. United States*, 249 U.S. 96 (1919), the Harrison Act was reinterpreted as having "the moral purpose of discouraging the use of drugs except as a medicine." This wording opened the door to the prosecution of doctors, because addicts were no longer considered patients, and thus satisfying their need for opioids could not be considered medical care. The Supreme Court thus agreed with a lower court's statement that "to call such an order for the use of morphine a physician's prescription would be so plain a perversion of meaning that no discussion of the subject is required." Thus the constitutionality of the use of the Harrison Act to enforce legal penalties on physicians who prescribed addictive medications to addicts was established. Over the next 14 years more than 77,000 violations, mostly by physicians, were prosecuted (Hohenstein, 2001). The Harrison Act was eventually repealed in 1970. The Controlled Substances Act was introduced that year, giving rise to the U.S. Drug Enforcement Administration (DEA) in 1973. In the late 1990s, stories of iatrogenic OxyContin addiction and the well-publicized arrest of overprescribing doctors continued to perpetuate unease over prescribing opioids for the management of chronic pain.

CAUSES OF ADDICTION

Exactly how great a role an exposure to drugs has in causing addiction is a source of continued controversy. The etiology of addiction is thought to be multifactorial. For instance, research into heredity suggests that there is often a strong genetic component. Studies of families in which many members are alcoholic have confirmed that addictions, especially alcohol dependence, run in families. However, genetic analysis has not shed light on which genes, or how many genes, are involved, and the relative contribution of genes versus environment is still actively debated, but it is clear that genes are important. They may determine, for example, how much dopamine is released after a person ingests a standard drink (Yoder, 2005). Also important is early, teenage, binge drinking. Studies in the early 2000s showed that addictions tend to be diseases with a clear pediatric onset, and adolescent drinking is a major culprit (Bonomo, 2004). There is

also evidence suggesting that psychological trauma and chronic stress can be contributory (Brady, 2005).

However, the question of whether opioids, stimulants, and other so-called "addictive" medications can themselves cause iatrogenic addiction is still being debated. Certainly these drugs can trigger a relapse in those already diagnosed with addiction, and they can possibly trigger addiction in those who are predisposed to it. Less clear is whether they can cause iatrogenic addiction in those without risk factors. An oft-quoted study from the 1980s estimated addiction to be as low as 5 percent in nonmalignant chronic-pain patients (Portenoy, 1986). However, a more recent meta-analysis looking at only the most valid studies found a prevalence of lifetime substance use disorders among this population ranging from 36 percent to 56 percent, and current substance use disorders were found to be as high as 43 percent (Martell, 2007). Whatever figure is believed or accepted, the true incidence of addiction in opioid-treated patients with chronic pain is unknown.

THE EFFECTS OF ADDICTION

There is evidence that chronic exposure to addictive drugs can have long-lasting effects on the brain. For example, drugs such as opioids and stimulants can alter dendritic density and branching. Furthermore, long-term use may reorganize brain circuits, moving the focus away from circuits associated with "reward" to those related to "habit" in the more dorsal parts of the striatum. This may explain why people with the disease of addiction keep using drugs, despite the loss of the ability to experience pleasure from drugs (Koob, 2003). A 2004 study suggests the possibility that chronic exposure to trace opioids may result in neuroplastic changes in the brain that may predispose to addiction (Gold, 2004). This study points out that while only 5.6 percent of licensed physicians in Florida are anesthesiologists, nearly 25 percent of those with substance abuse or dependence are anesthesiologists. The authors show that fentanyl, a powerful opioid, and anesthetics such as propofol are exhaled in measurable amounts by patients under general anesthesia. Further, in the operating room, direct exposure is common through inhalation, spilling, and "cracking off" the glass top of the vial containing the anesthesia drug. An intriguing hypothesis proposed by Gold is that long-term exposure to these opioids may sensitize or change the brain, resulting in vulnerability to addiction and relapse.

Also intriguing is the possible damaging effect of commonly used sedatives and stimulants on the developing brain. Ikonomidou et al. (2001) have shown that many commonly used anesthetic agents that are NMDA receptor antagonists or $GABA_A$ agonists may induce apoptotic neuronal cell death if administered to patients under the age of four, possibly resulting in later behavioral disturbances. Other studies, though controversial, on the use of stimulants in children being treated for attention deficit hyperactivity disorder (ADHD) have suggested that stimulants may reduce the incidence of the development of later addiction in this population (Beiderman, 2008).

PREVENTION

Given the uncertainty and controversy over the relationship between "addictive" but potentially helpful medications and iatrogenic addiction, the correct approach remains elusive, and always subject to change as our knowledge increases. However, some recommendations and observations can be made. Intensive screening for addiction and risks factors is warranted in patients being considered for potentially addictive medications such as opioids, benzodiazepines, and stimulants. Questions regarding any personal or family history of addiction, tobacco use, and social history can be very enlightening. This can also be problematic, however, since addiction carries stigma, and patients may not be forthright about their personal or family histories. Collateral information may be very helpful, especially since denial and minimization are hallmarks of addiction.

Physicians who treat pain, anxiety, and ADHD should have a low threshold for consulting an addiction medicine specialist to help evaluate and care for these often challenging patients. ASAM is working on the development of a core curriculum to address the overlap between pain management and addiction medicine. Innovative multidisciplinary clinics and rehabilitation facilities are needed that address both pain and addiction. Patients with the disease of addiction may also suffer from a chronic pain condition. These conditions can be successfully comanaged with appropriate medication choices and vigilant monitoring for compliance and recovery.

Finally, medications can be chosen to minimize their addictive potential. Since reinforcement is related to the rapidity of drug increase, medications that are time released, or have long half-lives may be less addictive than quick-release short-acting medications. For this reason, although breakthrough short-acting pain medications are sometimes helpful, they should be used sparingly. Nonreinforcing adjuncts are helpful, and urine monitoring for medications that should be present (as well those that should not) is suggested. If stimulants for ADHD or benzodiazepines for anxiety are warranted, long-acting medications may be preferred.

More research is clearly needed into the potential for iatrogenic addiction as a result of occupational exposure. Operating rooms should be well ventilated, scavenger systems operational, and gloves worn. Finally, addiction should be viewed as a life-threatening disease rather than a moral shortcoming. Those who suffer from it deserve to be treated with compassion and dignity.

See also **Addiction: Concepts and Definitions; Harrison Narcotics Act of 1914; Physicians and Medical Workers, Substance Abuse among.**

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IBOGAINE. The roots of the shrub *Tabernanthe iboga* first aroused pharmacological interest in 1864 when a French naval surgeon brought some back from Gabon, West Africa. The root was eaten by various Gabonese tribes as part of initiation ceremonies of puberty and was said to produce intoxication, visions, and a reduced need for sleep.

An active alkaloid, ibogaine ($C_{20}H_{26}N_2O$), was isolated in 1901 from the roots, bark, and leaves of *Tabernanthe iboga*. In the early 1900s, some medical researchers in France recommended ibogaine for use in treating neurasthenia and asthenia (syndromes that would probably be diagnosed in the twenty-first century as depression or fatigue syndrome). Although the drug was part of a proprietary medication marketed in Europe in the late 1930s and throughout the 1940s, ibogaine attracted little medical or scientific attention until the emergence of interest in indole alkaloids that accompanied the use of reserpine in the 1950s. During the 1960s, when there was considerable research on the use of lysergic acid diethylamide (LSD) and other psychedelic agents (hallucinogens) in psychotherapy, ibogaine was also studied, since it appeared to produce mental effects similar in some ways to other hallucinogens. At about the time of these studies, 1967–1968, the World Health Organization and the U.S. Food and Drug Administration (FDA) classified ibogaine as a hallucinogen, along with LSD, mescaline, and psilocybin.

In 1962, Howard Lotsof, who was at the time addicted to heroin, ingested ibogaine in search of a different drug experience. Lotsof came out of a long psychedelic experience, during which he had not taken any heroin, and found that he had no withdrawal symptoms and did not crave drugs. At the time, he noticed that ibogaine had a similar effect on several other heroin addicts. He subsequently remained drug free, completed law school, eventually obtained a patent on the use of ibogaine for the treatment of addiction (brand name Endabuse), and became active in seeking funding to urther develop the drug and to obtain FDA approval for its medical use in treatment of addiction.

As a Schedule I drug under the Controlled Substances Act, ibogaine is considered to be highly subject to abuse and without any approved medical use. To be approved by the FDA, an agent must be shown to be safe and effective. The only reports of the efficacy of ibogaine have been anecdotal ones from individuals in Europe who were addicted to heroin, cocaine, and tobacco. Those who take ibogaine are generally highly motivated since the drug is expensive, costing up to several thousand dollars. While many reported a decrease in drug craving after taking ibogaine, relapse to drug use within a few months was also observed.

As a result of pressure from activists, the U.S. government funded animal studies of ibogaine's actions on opioid and cocaine withdrawal, opioid and cocaine self-administration, and neurotoxicity. Studies in animals have not been entirely consistent. High doses of ibogaine reduced some manifestations of opioid withdrawal in monkeys. Studies in opioid-dependent rodents have shown that ibogaine decreases withdrawal, but other studies have not. Some rodent studies have shown a decrease in drug self-administration. Studies of ibogaine toxicity have also produced mixed results. Some studies in monkeys produced no obvious nervous system toxicity, but a study in rats produced damage to neurons in the cerebellum, the part of the brain known best for its role in control and coordination of movement. Other research studies indicate that ibogaine is not similar to opioids such as morphine and heroin nor to hallucinogens such as LSD in terms of actions at drug receptors.

Despite these inconclusive research findings, the National Institute on Drug Abuse (NIDA) has sponsored studies to evaluate the pharmacology and toxicology of ibogaine. The FDA has not approved ibogaine for treatment of addiction and NIDA discourages human trials. At least twelve

deaths have been attributed to the use of ibogaine in the treatment of heroin addiction.

See also **Ayahuasca; Hallucinogenic Plants; Hallucinogens; Treatment, Pharmacological Approaches to: An Overview.**

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IMAGING TECHNIQUES: VISUALIZING THE LIVING BRAIN.

The term *brain imaging* is most broadly used to encompass all non-invasive methods that depict internal features of the brain. Those most typically associated with imaging of the brain for studies of substance abuse and dependence are single photon emission tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging (MRI), and magnetic resonance spectroscopy (MRS). Each of these four major categories of techniques possesses strengths and weaknesses and they are increasingly becoming complementary tools for investigating the brain. As a group, they have the capacity to measure the concentrations of neurochemicals and rates of metabolic pathways, quantify specific proteins such as subtypes of neurotransmitter receptors or transporters, assess blood flow, observe changes in the brain caused by alterations in brain function, and map connections among brain regions. They are increasingly being used to address the little-studied issues of gender differences (Cosgrove, et al., 2007). This entry describes the technological basis of the imaging techniques and with each, briefly describes examples that highlight particular strengths of the methods with regard to their ability to study substance use, abuse, and dependence.

SINGLE PHOTON EMISSION TOMOGRAPHY (SPECT)

This technique might be considered an x ray from the inside, so a description of the principle of x ray is useful for understanding SPECT. An x ray is created by shining a beam of x rays at an object. A photographic plate or digital detector is placed behind the object (a hand, for example). The tissue absorbs some of the x rays and reduces the film exposure behind the hand. Bone absorbs more x rays than soft tissue, so where there are bones, the film is less exposed. Upon development, the outline of the hand is visible with bones readily apparent inside.

SPECT imaging, by contrast, makes use of injectable radioisotopes placed in chemicals that are associated with particular features of interest in the brain, such as blood flow or benzodiazepine receptors. The radio-labeled compound is injected, travels through the blood stream to the brain, where it is taken up and trapped, ideally in proportion to the quantity of the protein target or physical effect that is being studied. The radioisotope atoms that are part of the injected chemical emit x rays, which are measured with an array of detectors around the head. When the measurements are analyzed to form images, one can determine the distribution of the isotope through the brain. The sensitivity of this technique is high enough to make the measurements of chemoreceptor binding in the brain. In new SPECT cameras, the resolutions, defined as the full-width of the signal at half the maximum amplitude from a small sample, are 6 to 8 millimeters,

which means that areas of the brain that small and in some cases a little smaller can be visualized.

Isotopes commonly used with SPECT include iodine-123 and technecium-99m. A laborious and creative task for radiochemistry is the design of compounds that bind to brain targets at low concentrations, allow labeling with radioisotopes, and can enter the brain in sufficient quantities to allow their detection at doses that are safe for humans. Once promising chemicals are identified, additional work is carried out to measure whether the chemical's binding is specific enough to be useful and whether it yields sufficient sensitivity to support brain studies at safe concentrations.

SPECT is in use to study the effects on the brain of many drugs, including nicotine. For example, smokers have more nicotinic acetylcholine receptors than do nonsmokers (Staley et al., 2006). Among alcoholics, those in early abstinence show elevated benzodiazepine receptor numbers compared to nondependent healthy subjects, with nonsmokers showing greater elevations than smokers (Staley, 2005).

POSITRON EMISSION TOMOGRAPHY (PET)

Conceptually related to SPECT, the radioisotopes used with this technique do not themselves emit the x rays for detection by the scanner. Instead, they emit positrons, which are the positively charged equivalent of an electron. The positron travels randomly for up to a few millimeters until it encounters an electron, at which point the positron and electron annihilate one another and from the site of the collision, two x rays are emitted in almost exactly opposite directions. The PET camera has detectors around the head. A count is registered when two x rays are detected simultaneously 180 degrees apart. Background radiation is a source of noise in PET and SPECT imaging, and the requirement that detection be simultaneous at opposite detectors decreases the likelihood of random counts and increases the spatial resolution of the detection, with machines available as of 2008 with resolution of 4 to 5 millimeters.

PET is most commonly used to measure the uptake of the sugar glucose. Under most circumstances, glucose provides the primary fuel for brain energy metabolism. The analog of glucose, deoxyglucose, is taken into cells and almost entirely trapped by the first step of glucose metabolism, so by injecting radio-labeled deoxyglucose and mapping the radioactivity in the brain, one can measure how quickly various regions of the brain are using glucose, as developed in pioneering work by Louis Sokoloff and colleagues in 1977 and adapted and validated for use in humans in 1979 by Michael Phelps and coworkers with the positron emitter fluorine-18 in fluoro-deoxyglucose (FDG). FDG-PET is as of 2008 used widely to investigate cerebral metabolic changes that occur in substance abuse and other psychiatric disorders. Other isotopes that have found use are carbon-11 and oxygen-15.

Carbon-11 and oxygen-15 can be useful because those elements are common in many biological compounds. For example, instead of the glucose analogue FDG, it is possible to use glucose labeled with carbon-11, which is chemically identical to naturally occurring glucose in the body. Oxygen-18 can be used to create labeled water and image its uptake into the brain tissue as a measure of blood flow. A technical difficulty with some isotopes, including carbon-11 and oxygen-15, is their short radiological half-life, 20 minutes and 122 seconds, respectively. Facilities that use such short-lived isotopes must have a cyclotron on site to generate the isotopes immediately before each measurement.

These and other radioisotopes can be used to create ligands used to study dopamine release, dopamine receptor binding, serotonin receptor binding, and many other systems that are of interest for substance abuse. One example of PET applied to improve the understanding of addiction and craving was of dopamine receptor binding in cocaine-addicted patients (Wong et al., 2006). The results showed that the more each individual craved cocaine, the more dopamine that individual had bound to dopamine receptors. The authors concluded that there was likely to be more dopamine release in response to cues in strongly craving subjects than in those who craved cocaine less. Amphetamine, cocaine, and many other drugs of abuse share some effects on dopamine neurotransmission, and this piece of information about cocaine was anticipated to have relevance to craving for alcohol, nicotine, and other drugs.

MAGNETIC RESONANCE IMAGING (MRI)

As a technology that is ubiquitous in the industrialized world and is spreading through the developing

world, MRI has gained widespread utility for clinical evaluations of numerous disorders. MRI is also used widely as a research tool. Because it uses no ionizing radiation, it is often a method of choice for studying children and for following people sequentially over time to track the course of disease development or therapeutic effects.

MRI uses magnetic fields that are tens of thousands of times stronger than the earth's field. Certain atomic nuclei, including hydrogen, have a property called *spin*. When nuclei with spin are put into such a strong magnetic field, a very small minority, much less than one tenth of 1 percent, become aligned with the magnetic field. This small minority provides the sensitivity of the technique. Because the minority is so small, MRI is a relatively insensitive method, on a per-atom basis, but because hydrogen is so abundant in the body, MRI is able to provide measurements of less than one cubic millimeter. If energy is applied to the head in very brief bursts, typically microseconds or milliseconds in length, the nuclei change their distribution. As they gradually return to their slightly biased orientation in the magnetic field, they emit energy, and this energy is detected and used to make images. The frequency of the energy transmitted to the head and received from the head depends on the magnetic field strength and generally lies in the FM radio band. For this reason, MRI suites are generally shielded against outside radio signals, which appear as noise in MRI. A typical hospital MRI machine uses a 1.5 Tesla magnet that operates at 60 MHz, or increasingly, a 3 Tesla magnet that requires 120 MHz, and the frequency of operation depends directly on the magnetic field strength. Stronger magnets are in use for human research projects, as of 2008 as high as 9.4 Tesla. The rate of return to the orientation in the magnetic field is governed by the physical property called *T1*, and the rate at which their radiofrequency signal dies away is under the control of the property called *T2*. T1 and T2 are called *relaxation times*, and their respective values in the brain are typically measured in seconds (for T1) and tens to hundreds of milliseconds (for T2).

A magnet and radiofrequency transmission and reception are sufficient to measure a signal, but not to make images, which requires mapping the locations where the signals originate. MRI machines are equipped with what are called *gradient coils* that are used to induce magnetic field *gradients*. When electric currents pass through the gradient coils, they create linear ramps to the field of the large magnet. Because the frequency of reception at a given location depends on the magnetic field strength at that place in the brain, it is possible in the presence of gradients to determine where in the brain a signal arose, by determining the precise frequency of the signals. The gradient coils are also responsible for most of the loud noises that emanate from MRI machines. Gradient coils make MRI feasible for clinical work and human research, and for their dramatic breakthroughs Paul Lauterbur of SUNY Stonybrook and Peter Mansfield of Nottingham, England, shared the 2003 Nobel Prize for Physiology or Medicine.

Although MRI uses no ionizing radiation, there are risks to its use that must be considered carefully. The primary risk is that of metallic objects being pulled toward the magnet. Such an object could be an iron-containing tool that flies toward the scanner, injuring anyone in its path, or it could be an implanted metal object such as an aneurysm clip. Also at risk are electronic implants that may malfunction in the magnetic field, such as a pacemaker. As magnetic field strengths rise, it has become more important than ever to verify the MRI-safety of implanted medical devices. Some devices are said to be MRI safe, but they may only have been approved for use at magnetic field strengths of 1.5 Tesla, and not above. Some have been approved for use at 3 Tesla, but each device should be checked for safety at any magnetic field.

MRI can be subdivided into structural, functional, perfusion, diffusion, and under development as of 2008, molecular imaging, and magnetic resonance spectroscopy. Each is unique in its application and is discussed below as a separate imaging modality. What is common about each is its goal to create contrast to distinguish particular features of interest.

Structural MRI. This most common form of MRI provides anatomic information about the brain. The images generally resemble what would be seen in an anatomy text, but acquisition parameters and methods can be tailored to emphasize particular aspects, such as vasculature (blood vessels) or fluid-filled lesions (such as areas of dead

tissue), for examples. Image contrast often uses the T1 and T2 relaxation times to differentiate tissue, with what are called T1- or T2-weighted images. Images can be obtained under conditions that black out tissues with long T1 values, such as fluid, so that the ventricles (fluid-filled structures in the brain) and sulci (fissures in the surface of the brain) appear black in an image, and the rest of the brain is light. Images can also be measured in ways that emphasize tissues with long T2 values, such as fluid that fills small strokes in the white matter. Contrast agents as of 2008 function primarily by shortening the T1 relaxation time in their vicinity and may be introduced to delineate where the blood-brain barrier has been compromised by acquiring images with scanning procedures that show brighter features where T1 is reduced by the contrast agent.

In research projects, structural images are sometimes used to rule out neurologic contraindications for study participants, but many studies use structural MRI as the primary goal, obtaining measurements of volumes and shapes of brain regions in disorders of the brain. For example, it is possible to measure the thickness of the layer of gray matter that covers the brain, or the size of the fluid-filled ventricles inside the brain, the total volume of white matter in the brain, or the size of particular regions like the frontal lobes or the hippocampus.

MRI image intensity varies according to the type of tissue present (cerebral spinal fluid, white matter, gray matter, or abnormalities such as strokes). The MRI contrast can also depend on factors such as proximity to the ears, the sinuses, the mouth, or deposits of iron in the brain. Any factor that disrupts the magnetic field in the brain has the potential to distort the signal and reduce the image intensity near the object. A bobby pin lodged firmly in a subject's hair might not move in the magnetic field but would eliminate the signal from large regions of the brain. Likewise, deposits of iron in the cerebellum can darken the image at the site of the deposits. Boundaries between air and tissue, as occurs in the sinuses or the ear canals, also can lead to image darkening. These factors must be considered when analyzing structural MRI.

Structural MRI has been used to observe changes in the brain in a variety of disorders. MRI showed reduced volumes of the frontal cortex in recently abstaining cocaine addicts (Fein et al., 2002) and smaller hippocampus and amygdala in marijuana smokers (Yucel et al., 2008). Heavy drinkers have reductions in brain volume that recover significantly after the patients stop drinking, although the recovery is less in tobacco smokers (Gazdzinski, 2008). Indeed, knowledge of that recovery often gives hope to alcohol-dependent patients seeking treatment, providing them with tangible evidence that sobriety will quickly change something so measurable as the sizes of structures in their brains. These are only three examples in the early 2000s of the numerous applications of structural MRI to research on substance abuse.

Functional MRI (fMRI). A common MRI research tool for studies of substance abuse and dependence is fMRI. Most fMRI depends on blood oxygen level-dependent (BOLD) contrast and depends on the magnetic susceptibility caused by deoxygenated hemoglobin (Ogawa et al., 1990; Kwong et al., 1992). Deoxygenated hemoglobin distorts the magnetic field locally and thereby reduces the image signal intensity in its vicinity, whereas oxygenated hemoglobin does not. When blood oxygen levels drop, the MRI signal intensity nearby decreases, and when blood oxygen increases, the MRI signal rises. One might expect, then, that if brain function increases in a particular region of the brain, the brain energy requirements will rise, oxygen levels will be reduced in the nearby capillary bed, and the MRI signal would drop. Paradoxically, however, the MRI signal increases when brain activity increases, and this occurs because blood flow rises rapidly and compensates with oxygen beyond the tissue's immediate needs. Therefore, MRI can be acquired under different conditions, often taking measurements in tens of milliseconds. The images acquired during different activities can be compared, and areas in which intensity changes are observed are designated as having been affected by the change in functional state. Using the principles of the changes in image intensity, brain activity can be evaluated with respect to functional tasks, pharmacologic influences, and changes caused by disease states.

When evaluating an fMRI study, some factors must be considered. One factor is the baseline state, because fMRI necessarily compares two conditions.

For example, if a higher BOLD response is observed in the dorsolateral prefrontal cortex during a functional challenge in a cocaine addict relative to a healthy comparison subject, it could be that the patient required more functional activity to achieve the same task, or it could be that the patient had a lower baseline activity than the control subject but used the same amount of energy to perform the task. Another important factor to consider is that although the contrast is called BOLD, the signal change results not only from the blood oxygenation, but also from the blood volume and the rate of blood flow in the vicinity of the activation. Blood flow or volume can themselves change the BOLD response either independently or interactively with function. Pharmacologic agents (medications) or disease states may therefore alter fMRI findings by themselves. An fMRI is sensitive to brain function but must be interpreted carefully since it is also sensitive to misleading interpretation.

Although structural MRI generally provides information about long-term conditions and changes, fMRI may also be used to assess acute effects. One such example is a study of methadone treatment for heroin addiction that showed significant brain functional responses to heroin-related cues and that methadone reduced those responses (Langleben et al., 2008). The finding is consistent with a vulnerability to relapse that is greatest shortly before the daily dose of methadone. A different strategy to evaluate substance abuse is to use a compound that mimics particular aspects of a substance, like using ketamine to simulate some glutamatergic effects of alcohol, in which case fMRI studies of ketamine (Honey et al., 2005) may provide insights into alcoholism (Krystal et al., 2003; Petrakis et al., 2004).

Perfusion MRI. As a research tool, perfusion MRI can be achieved by various means. Prevalent as of 2008 is a non-invasive approach that uses radiofrequency to effect changes in blood water signal selectively in the neck and then acquire images in the brain. Cerebral perfusion can be assessed by the appearance of the altered blood signal arriving in image slices. Perfusion MRI has been combined with pharmacologic challenges to create *pharmacological MRI* (phMRI), and it has been combined with functional challenges for purposes similar to what is done with fMRI: for example, to determine how brain perfusion changes before and after a drug is administered.

Perfusion MRI has been used to investigate a variety of substances. One study of cocaine abusers took the novel step of using both SPECT imaging of blood flow and perfusion MRI. Both methods showed significant reductions of blood flow in several deep brain regions and in frontal white matter (Ernst et al., 2000). This study illustrates the benefits of combining imaging techniques and highlights the impact on white matter in psychiatric diseases in general and substance abuse and dependence in particular.

Diffusion MRI. As was illustrated in the discussions of deoxygenated hemoglobin and the presence of magnetic objects, one of the factors that reduces the signal in MRI is magnetic field disruption in some part of the image. Imagine, then, that on a microscopic scale, some water molecules wander randomly from one location to another, where the magnetic field is slightly different. The signal from that water molecule will be lower. Typically, the magnetic field does not vary so strongly on a microscopic scale, but gradient coils can be used to apply a deliberate disruption of the field. The stronger the magnetic field gradient applied, the greater is the sensitivity of the method to the movement of the water molecules, so water that is able to move more freely has its signal reduced. It is possible to apply gradients in different orientations to assess the directionality of the water diffusion. Under those circumstances, one can evaluate the loss of structure in the tissue (diffusion anisotropy) and carry out fiber tracking to evaluate connections among brain regions.

Numerous applications of diffusion MRI have been used, many with diffusion anisotropy rather than the more computationally demanding fiber tracking. Among them is a study of children exposed prenatally to cocaine, which showed that poorer cognitive functioning was directly related to greater fractional anisotropy in frontal white matter (Duckworth Warner et al., 2006). White matter in the normal brain is highly structured, with fibers running from one part of the brain to another. Anisotropy in this case represents a breakdown of that organization in the white matter, perhaps by loss of fibers or by less uniform orientation of fibers in the white matter. This example was selected

because it demonstrates the use of MRI in children and because it targets themes that are repeated in investigations of drugs of abuse: damage to white matter and loss of white matter organization.

Molecular Imaging. An area of MRI with enormous potential is the use of contrast agents that target particular chemical receptors or reactions and change image intensity once at the target. Approaches to molecular imaging as of 2008 include the tagging of iron to chemicals that bind to targets of interest in the brain, analogous to the radio-labeling strategies of SPECT and PET: where the iron goes, the signal amplitude is reduced in the images, so MRI darkening represents the presence of the tagged chemicals. Another approach is to use genetic engineering to introduce a protein that can convert an inactive contrast agent to an active one, so that the contrast agents will be effective in cells that express the new gene. Such a gene can be introduced linked to a section of DNA of interest, so that cells that are affected by the contrast are known to carry the section of DNA. A new approach as of 2008 is imaging of transcription of messenger RNA from DNA, which is the first step toward protein synthesis (Liu et al., 2007): This technology allows the mapping of mRNA non-destructively in animals and holds potential for helping researchers understand the processes of drug addiction, treatment, and recovery at the level of generation of RNA from DNA for particular proteins.

MAGNETIC RESONANCE SPECTROSCOPY (MRS)

Magnetic resonance has the ability to measure multiple distinct neurochemicals at the same time. To be detected, chemicals typically must have concentrations of at least a few hundred micromolar, with most scanners limited to 0.5 millimolar or more, but even so, the approach can yield measurements of important chemical entities. The primary chemicals detected by MRS are N-acetylaspartate (NAA), creatine combined with phosphocreatine (Crtotal), a combination of choline, phosphorylcholine, and glycerophosphorylcholine (Cho), myoinositol, and glutamate, glutamine, and gamma-amino butyric acid (GABA). The latter three are usually detected as a combined set of chemicals called *Glx*. With specialized techniques, it is possible to measure GABA, glutamate, and glutamine separately from one another, but the approaches as of 2008 still require some specialized implementation. NAA is found in neurons, and its purpose as of 2008 is not established, although it is known to decrease when neuronal health is compromised, often recovering with clinical improvement. Crtotal is a crucial element in energy metabolism, but because creatine is not resolved from the energy-rich form, phosphocreatine, Crtotal provides little information about energy states. Choline is generally believed to reflect membrane breakdown and or synthesis. Glutamate, glutamine, and GABA are closely interrelated through energy metabolism and neurotransmitter release and uptake, although their total levels have not yet been related to rates of neurotransmitter release.

An example of the utility of MRS in studying children was an evaluation of effects of cocaine exposure during gestation. Although structural MRI showed no abnormalities, creatine levels were 13 percent higher in the children exposed to cocaine (Smith et al., 2001). MRS can also be used to investigate acute effects of drugs, such as acute changes in brain GABA induced by the nicotine after smoking and drinking.

The neurochemicals discussed are all detected by monitoring the hydrogen signature of the brain, but phosphorus metabolism can also be assessed with MRS, allowing the detection of high-energy phosphates such as ATP in the brain, as well as phosphomonoesters and diesters. A newer and novel technology is carbon MRS, which detects the nonradioactive isotope carbon-13 that occurs naturally as 1 percent of all carbon. Because the natural carbon signal is so low, it is possible to inject glucose, acetate, or other compounds labeled with the material and using MRS observe the gradual increase of glucose products in the brain, including glutamate, glutamine, and GABA. The more rapid is the labeling, the faster the rate of synthesis. The kinetic information (reflecting changes in concentration over time) obtainable with carbon-13 MRS holds promise for understanding the effects of substances of abuse on amino acid neurotransmission and energy metabolism, but such applications are as of 2008 in their infancy.

Technology development continues for all of the methods of imaging described in this entry. For PET and SPECT, new chemicals are continuously under development and testing is being done to

target particular proteins more effectively at lower doses, or with better time resolution, or with greater specificity. PET and SPECT are constantly pushing for higher spatial resolution (to provide clear images of smaller brain areas), as are MRI techniques. For MRI, improvements in sensitivity occur as magnetic field strengths rise and as the technology for coil designs, transmission, and reception improves. Great excitement has arisen in the early 2000s in the MR community over hyperpolarized carbon-13. Although it has not been shown as of 2008 to be useful for metabolic studies of the brain, its success in studies of other organs and in cancer leave the possibility open for new solutions to allow its effective application to studies of the brain in general and substance abuse in particular.

See also **Brain Structures and Drugs; Reward Pathways and Drugs.**

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GRAEME F. MASON

IMMUNOASSAY. Immunology is a laboratory science that studies the body's immunity to disease. The basic mechanism of immunity is the binding of drugs or other chemical compounds to antibodies (large proteins produced by the body's immune system). An assay is a general term for an analytical laboratory procedure designed to detect the presence of and/or the quantity of a drug in a biological fluid such as urine or serum (the fluid component of the blood obtained after removal of the blood cells and fibrin clot). An immunoassay, therefore, is an analytical procedure which has as its basis the principles of immunology—specifically the binding of drugs to antibodies.

Several different types of immunoassay are routinely performed in the laboratory. Although they differ in the types of reagents and instrumentation used, they are all based on the same scientific principle (the binding of drugs to antibodies). The three types of immunoassay that are commonly used for drug testing are the radioimmunoassay (RIA), enzyme multiplied immunoassay (EMIT), and fluorescence polarization immunoassay (FPIA).

It may facilitate the reader's understanding of immunoassay to envision the reactions that occur in the body following a vaccination (e.g., polio). The vaccine contains a weak or a killed solution of (polio) virus. When the vaccine is injected into the body, the immune system recognizes the presence of a foreigner (the polio virus), and it generates antibodies to that virus. These antibodies circulate in the blood, and they constitute the body's protection; if at some later date a live (polio) virus invades the body, the antibodies recognize it by its unique size and shape (similar to the fit of a lock and key); they spontaneously bind to the virus, leading to its inactivation and removal from the body.

This binding of antibodies to drugs forms the basis for immunoassay. In the development of an immunoassay, the first step is to inject an animal (host) with the drug that we ultimately wish to analyze. The host immune system, recognizing the drug as a "foreigner," generates antibodies to this drug, and these antibodies can then be harvested from the serum of the animal. In the test-tube environment of the laboratory (*in vitro*), these antibodies can be recombined with the appropriate drug. Just as it did inside the body (*in vivo*), the antibody will recognize the drug based on the lock-and-key fit and will spontaneously bind to it.

The second step in the development of an immunoassay is to synthesize a "labeled" drug. This involves the chemical addition of a "marker" to the drug. This marker can be small, such as an atom of radioactive iodine, or it can be large, such as an enzyme, which is a fairly large protein. Irrespective of its size, this marker is added in such a way that it does not interfere with the lock-and-key recognition between the antibody and the drug.

Commercially available immunoassay kits contain the antibody (which the company has prepared as described above) and the labeled drug (which has been chemically synthesized) necessary to perform the assay. In the laboratory, a fixed amount of antibody and a fixed amount of labeled drug are placed into a reaction vessel (test tube). If these were the only two ingredients, all the binding sites on the antibody would react with (bind to) the labeled drug. A third ingredient added to the assay is, however, the unlabeled drug (i.e., the urine, saliva, or serum specimen containing the drug that is being measured). Because the label on the labeled drug is placed in a position that does not interfere with binding to the antibody (i.e., it is "hidden"), the antibody cannot distinguish between the labeled and unlabeled drug.

Immunoassays are always designed so that there are fewer antibody-binding sites present in the reaction mixture than there are molecules of (labeled plus unlabeled) drug. Because the labeled and unlabeled drug appear the same to the antibody, they will compete equally for the limited number of available binding sites on the antibody. By measuring the amount of labeled drug bound to the antibody, the analyst can calculate the amount of unlabeled drug in the biological specimen.

All immunoassays work in the same basic fashion. They differ in the types of labels that are added to the labeled drug and in the analytical methods by which the amount of binding of labeled drug to the antibody is measured.

RADIOIMMUNOASSAY

Radioimmunoassay (known as RIA) was the earliest of the immunoassay techniques. It was developed during the 1950s by a pair of research immunologists in New York City, Dr. Solomon A. Berson and Dr. Rosalyn S. Yalow. Their initial RIA was designed to detect very low blood levels of insulin and they published their findings in 1959. Their development of this technique was considered of such importance to science that Dr. Yalow was awarded a Nobel prize in 1977 for their work (since Dr. Berson died in 1972 and Nobels are not awarded posthumously, Berson's contribution was remembered in Yalow's acceptance speech).

In RIA, the marker is an isotope of a radioactive element, hence the name *radio*immunoassay. In most RIAs performed in the laboratory today, the radioactive isotope used as the marker is iodine 125, although tritium (hydrogen 2), carbon 14, and cobalt 57 are used in some assays. RIAs can be used in two different fashions to give information about the drug in a sample: (1) they can be used qualitatively—to determine whether a drug is present or absent (e.g., in urine drug testing); (2) they can be used quantitatively—to determine how much of a drug is present (e.g., to measure serum levels of drugs such as digoxin, a heart medication, or theophylline, an asthma medication).

RIA is an extremely powerful tool. One of its main advantages is the sensitivity that can be achieved. Drug levels in serum and urine that are as low as 10 to 100 parts per billion are routinely measured. Two of the most sensitive of the radioimmunoassays are the urine LSD assay and the serum digoxin assay, both of which can detect less than one part per billion. RIA is also an extremely versatile tool. It is used to measure a wide range of drugs of abuse in blood, serum, saliva, and urine, as well as therapeutic (physician administered) drugs in blood or serum. It is also used as a diagnostic tool to detect and quantify numerous naturally occurring chemicals in human serum and urine. Another characteristic that makes RIA such a powerful tool is the specificity of the assay. The antibodies are highly specific for the drugs analyzed and they rarely make a mistake in recognizing the lock-and-key fit between antibody and drug.

One of the major limitations of the radioimmunoassay is that it generates radioactive waste. To avoid spreading the radioactive compounds and contaminating the environment, the laboratory must conform to very strict regulations, including very elaborate procedures for waste disposal—and undergo frequent inspections. Because of a short half-life for some isotopes, another limitation is that the reagents with a radioactive label have a short shelf life. For instance, the majority are RIAs labeled with iodine 125; they have a shelf life of only approximately sixty days.

Some very sophisticated automated equipment is available for performing RIA or, if need be, the assays can be performed manually. All RIAs require the use of an instrument called a gamma counter, which measures the amount of gamma radiation given off by the radioactive drug bound to the antibody. In 2008, gamma counters could be purchased for several thousand dollars. The reagents are moderately expensive (costing from less than fifty cents per test to two to three dollars per test, depending on the specific assay and the volume of reagents purchased).

ENZYME MULTIPLIED IMMUNOASSAY

The enzyme multiplied immunoassay technique, also known as EMIT™, is a variation of the general immunoassay technique, in which the marker used to prepare the labeled drug is an enzyme, rather than a radioactive isotope. EMIT is a two-stage assay. As in the other immunoassays, the sample, which contains some amount of the drug being measured, is combined with the antibody plus a fixed amount of the enzyme-labeled drug. In the first reaction, the labeled and the unlabeled drug compete for the available binding sites on the antibody (standard immunoassay reaction). A secondary reaction is then performed, which involves only the enzyme portion of the labeled drug. The results of this secondary reaction are used to calculate the amount of enzyme-labeled drug that is bound to the antibody and thus how much (unlabeled) drug there was in the original urine or serum specimen.

As with other forms of immunoassay, the EMIT can be used either qualitatively or quantitatively. In

urine specimens, it is used to detect the presence of drugs, such as THC (marijuana), cocaine, PCP, opiates (heroin), amphetamines, and barbiturates. In serum specimens, EMIT is used to determine the amount present of drugs used for therapeutic (medical) purposes. Such drugs include acetaminophen (Tylenol), salicylate (aspirin), theophylline (widely used to treat asthma), several drugs used to treat epilepsy, and several drugs used to treat heart abnormalities.

Advantages that the EMIT technology has over the RIA are (1) that no radioactivity is involved, so the waste is more readily disposable; (2) the reagents are relatively stable, which may be particularly attractive to a small laboratory, which runs only a few specimens. The EMIT reagents are also less costly than the RIA reagents. The basic instrumentation requires less capital outlay than does the RIA, however the expense grows as more sophisticated automation is acquired.

Some limitations of the EMIT technique are (1) that it is somewhat less sensitive than the RIA (in particular, the LSD assay requires detection of such minute levels of the drug in urine that it can only be done by RIA); (2) also, EMIT is less specific than RIA and is subject to some interferences that do not affect the RIA—for example, the EMIT assay for amphetamines in urine gives a positive response with several other drugs that are similar in structure to amphetamines.

FLUORESCENCE POLARIZATION IMMUNOASSAY

Fluorescence polarization immunoassay (known as FPIA) is a technique that was developed by Abbott laboratories and marketed under the trade name TD_X. As the name FPIA implies, the marker for the labeled drug is a molecule of a naturally fluorescent compound called fluorescein. The amount of labeled drug that binds to the antibody is measured by a sophisticated instrument called a spectrofluorometer. As with the other immunoassays, this measurement is used to calculate the amount of labeled drug bound to the antibody and thus the amount of drug in the original urine or serum specimen.

The instrumentation necessary to perform the FPIA is only made by Abbott. It is expensive to purchase (upwards of $50,000) but can be leased from the manufacturer. The reagents are more expensive than EMIT reagents, being roughly comparable in cost to RIA reagents. They come in a liquid form and have a more limited shelf life than those for EMIT, but they tend to be more stable than RIA reagents.

The attractiveness of FPIA is in the speed and ease of operation of the instrument. The reagents come in a kit that is bar coded and is placed right into the instrument. All the operator has to do is fill the sample cups with serum or urine, place the reagent pack inside the instrument, and push a button marked "run." The instrument reads the bar code, enters the necessary programs into its memory, performs the assay, and prints out the results. For the routine hospital lab or small drug-testing lab, it is as fast or faster than EMIT or RIA and a lot easier; however, the instrument can only run twenty specimens at a time. For the large drug-testing laboratory, more rapid results can be achieved with the automated instrumentation available for the EMIT or RIA techniques.

FPIA is nearly as sensitive as RIA; digoxin can be run by FPIA, although LSD is still not available. The specificity of FPIA is also comparable to that of RIA.

See also **Drug Testing Methods and Clinical Interpretations of Test Results; Hair Analysis as a Test for Drug Use.**

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JEFFREY A. GERE

IMPULSIVITY AND ADDICTION.

Impulsivity is a construct that has relevance to a broad range of psychiatric disorders and behaviors, including attention deficit hyperactivity disorder, bipolar disorder, substance use disorders, cluster B personality disorders (e.g., antisocial and borderline personality disorders), formal impulse control disorders (e.g., pathological gambling and kleptomania), and suicidal and other self-injurious behaviors. *Impulsivity* is defined as a predisposition toward rapid, unplanned reactions to internal or external stimuli with diminished regard to the negative consequences of these reactions to the impulsive individuals or others.

Impulsivity is a complex construct composed of multiple elements. Domains of impulsivity (e.g., those related to risk/reward decision-making, response disinhibition, and attention) have been identified in factor analyses. Measures of impulsivity often show little to modest correlations across these domains or are sometimes inversely related to one another. For example, rapid response has been shown to correlate inversely with disadvantageous decision-making in cocaine dependent subjects when they perform on some measures such as the Iowa Gambling Task. Behavioral and self-report measures of similar constructs within each domain of impulsivity also do not uniformly show expected correlations. For example, consider delay discounting, the process by which individuals temporally discount the value of rewards. More impulsive individuals tend to show greater preferences for small, immediate rewards as compared to larger delayed ones. The steepness of discounting of rewards can thus be considered a measure of impulsivity. However, individuals can report preferences for specific smaller immediate rewards as opposed to larger delayed rewards, though their responses may not correlate with real-life measures of preferred immediate versus delayed reward.

For example, self-report and behavioral measures of delay discounting were collected in adolescent smokers. The self-report measures asked about hypothetical reward preferences; for example, "Would you prefer US $54 today or US $55 in 117 days?" The behavioral task involved individuals sitting in front of a computer monitor and selecting immediate rewards (for example, 15 cents) or larger ones (for example, 30 cents) delayed for a period of time (for example, 30 seconds), with subsequent amounts adjusted according to the immediately preceding selection (for example, if the larger, delayed amount was selected, the immediate amount would increase). Self-report and real-life measures were not correlated with one another, and the real-life measures were associated with successful smoking cessation, whereas the hypothetical measures were not. These findings might parallel others in real-life settings, for example, with dieting behaviors, in which one might report placing a higher value on a delayed reward (better physical fitness) over a smaller immediate reward (dessert) but behave differently in the setting of being served a dessert.

Impulsivity has particular relevance to drug addiction and multiple stages of the process by which addiction develops. Animal and human studies indicate that impulsivity can predispose to experimentation with drugs and thus may be particularly relevant to initiation of drug use. Impulsivity has also been associated with relapse to substance use by addicted individuals. Measures of impulsivity and related constructs have also been associated with severity of and treatment outcome for psychiatric disorders. For example, measures of impulsiveness have been repeatedly found to be elevated in groups of individuals with pathological gambling, and decreases in gambling symptomatology have correlated with decreases in measures of impulsiveness. Brain imaging studies as of 2008 were beginning to identify specific aspects of brain circuitry that influence specific aspects of impulsivity and related constructs in mentally healthy and psychiatric populations, including those with addictions. Such approaches, particularly when integrated into treatment studies, were expected to

inform the development of improved prevention and treatment strategies.

See also **Risk Factors for Substance Use, Abuse, and Dependence: Sensation Seeking and Impulsivity.**

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MARC N. POTENZA

INDIA AND PAKISTAN. Intoxicants of various kinds have been used in the Indian subcontinent for millennia. Opium entered India through Arab medicine, cannabis was traditionally consumed in religious and social festivals, and alcohol was consumed despite the prohibitionist ethos of many of the subcontinent's religious traditions. The local trade in intoxicants was well established before the advent of European colonizers, but Portuguese and, later, British officials created sophisticated economic and financial networks rapidly increasing its scope.

Of the intoxicants consumed on the subcontinent, opium and its derivatives have received the most attention due to the continuing controversy over the Indo-Chinese opium trade and the region's contemporary role in trafficking narcotics. The impact of opium in the domestic market only began to be analyzed in the early twenty-first century, at least in the detail previously reserved for its export (Richards, 2002). Research into the consumption of other intoxicants, both licit and illicit, has also increased, so that a more balanced understanding of their long-term impact is emerging from under opium's shadow.

The Indian trade evolved into a complex business operation involving millions of people, from cultivators of the poppies to local merchant intermediaries, government factory workers, and laborers on to the docks of Calcutta and Bombay. Profits, naturally, remained skewed to the higher echelons, and they were more evenly distributed in the western districts of India. Nevertheless, opium remained an important element of the local economy as well as a major source of revenue for the East India Company (EIC), the British Government of India, and the western princely states.

EARLY USE OF OPIUM

Opium had been used as a medicine in India since its introduction by Arab traders**.** The eating of opium as a daily general tonic was widespread; however, unlike farther east in Asia, in India it was consumed in the form of tablets and liquors, and recreational opium smoking was viewed with distaste. Demand for Indian opium in China was rooted in its mellow taste. Indian opium had a lower morphia content of 3 to 6 percent compared to the domestic Chinese product and the 12 percent of Turkish opium, and its mellowness was much desired by smokers, in particular the mild Patna opium. As a result, the trade in Indian opium expanded rapidly (Winther, 2003).

At first, opium smoking in China was a form of medication against fevers, dysentery, and that nineteenth-century scourge, cholera. As the price was reduced throughout the century, usage expanded from the medical market to the country's poorer

classes. With the leaching of opium from medicinal use, the number of addicts increased, creating a near constant demand for Indian opium throughout the century. However, the trade was shrouded in controversy.

THE OPIUM TRADE

While the opium trade expanded—along with global trading in other intoxicants of the new consumer age, such as coffee—the commercialization of a narcotic ensured that the trade was couched in double standards. The East India Company board of directors insisted that company ships could not be involved in the trade after the Chinese Government placed embargoes on opium imports. However, the EIC ensured that there were ample supplies of good-quality opium from Patna for auction at Calcutta for the British and American merchants who smuggled the product into China. The company monopolized the production from field to factory to port, and it knew the final destination of the trade, but the profits available for the constantly cash-strapped EIC, which was tasked with acting as the de facto colonial government of India, were too high to resist.

Initially, the EIC did not gain from the Malwa opium trade in the West, which was in the hands of officials of the princely states and merchant and banking intermediaries. The desire to force the trade through Bombay and dent the independence of the princely states was part of the motive behind the British annexation of Oudh. Opium, therefore, was a key element in the expansion of the British Empire, both within and outside of the Indian subcontinent. When the Crown finally took control of the government of India in 1857, the profits of the opium trade were once again too attractive to forgo, despite an increasing clamor against the immorality of the commerce.

CANNABIS

Cannabis use was also rooted in medical systems in India, but was regarded as controversial by the colonists. Although William O'Shaughnessy (1809–1889), the editor of the *Bengal Pharmacopoeia* (1844), advocated cannabis as a powerful remedy in cases of rabies, tetanus, cholera and convulsive disorders, many early travelers commented upon its intoxicating effects and regarded its use as predominantly recreational and social rather than medicinal. The government's 1871–1872 report on cannabis linked its habitual consumption to an increased risk of insanity. Cannabis became a key element in the prohibitionist platforms, including that of the Society for the Suppression of the Opium Trade (SSOT). William Sproston Caine (1842–1903), a temperance reformer and member of the British Parliament, declared it to be "the most horrible intoxicant the world has ever produced," and the Indian government was demonized in prohibitionist circles for deriving substantial revenue from an intoxicant. While the opium trade was regarded as the public sin of the Indian authorities, their condoning of cannabis consumption was the private sin.

Cannabis aroused economic fears about the weakening of the India labor force, as well as social fears of the creation of a criminal class driven insane through the overconsumption of *ganja*. The resulting seven-volume Indian Hemp Drugs Commission Report of 1894 simply fuelled the controversy further. This commission, also known as the Young Commission, sat for over two years and heard 1,193 witnesses from throughout the subcontinent with widely diverging views. The report likened cannabis consumption in India to that of alcohol in Britain, arguing that as long as the latter was tolerated, the former must be as well. Indeed, the Majority Report decreed that the banning of *bhang* (cannabis liquor) was unjustified because it was far less potent than alcohol. While accepting that smoking *ganja* and *charas* (hashish), if consumed habitually and in sufficient amounts, was an activity potentially more addictive than drinking alcohol, the prohibition of these substances was rejected. Not only would it be regarded as an attack on the cultural and religious practices of the population, a ban would be counterproductive and simply lead to a search for other illicit, and possibly more potent, intoxicants. It would also raise the cost of policing.

THE POLITICS OF OPIUM

The controversy over governmental attitudes toward intoxicants increased with the publication of the Report of the Royal Commission on Opium in the following year. The Majority Report declared that opium was fundamental to government revenue in India and, through the Home Charges, to the British Government as well. Further, the use and trading of opium could not be banned because citizens of both

India and Britain would not accept the new taxes required to replace revenue lost from opium. The report also expressed skepticism that the Indian opium habit was necessarily harmful, deeming anti-opium propaganda exaggerated and unduly alarmist. So convincing were the arguments condemning a ban, that the former prohibitionist Arthur Pease was drummed out of the SSOT for signing the Majority Report. Temperance campaigners were horrified by both the cannabis and opium reports, declaring that the commissioners had been unduly influenced by financial over moral considerations.

With the rise of the use of Indian indentured servants and Indian seamen throughout the British Empire and beyond, local consumption patterns were exported around the globe. This helped to increase fears of narcotic criminality and degeneration. At the turn of the twentieth century, Indians would often appear in contemporary accounts of Chinese opium dens being used by missionaries, anti-narcotics campaigners, and politicians alike to condemn the "opium habit."

The Indian narcotics reports came in for excoriating criticism in a later report by the missionary Bishop Charles Brent in the Philippines, which formed the basis of American attempts to introduce international drug controls. By then, however, the government of India had accepted that the opium trade was prejudicial to its prestige, and it had already reached agreement with the Chinese government to end the opium trade between their nations over the next decade if the latter controlled its domestic production. Only five years later, the Indo-Chinese trade was ended, at a cost of approximately US $8 million to India. At the Hague Opium Convention of 1911–1912, the government of India agreed to end the opium trade to those countries, including the Philippines, in which an embargo on imports was already in place. However, if the West wanted any further concessions, India demanded that pharmaceutical-manufacturing countries be treated in the same way as producing countries, with the manufacture of morphine and heroin strictly limited to the amount required for medicinal needs. Such demands, naturally, were unpopular with these countries, which argued that their products were used strictly for medicinal purposes.

India's request for limitations on cocaine did not meet with any greater success. Such limitations would have impinged further upon the export trade of Western nations, and the government of India was accused of attempting to divert attention away from its role in the opium trade. However, both central and provincial authorities in India were concerned about the rising level of cocaine consumption. Cocaine was considered an intoxicant foreign to India, but it seemed to be taking a speedy hold of addicts in the major drug trafficking centers such as Bombay, Calcutta, and Rangoon. Indian authorities were among the first to try to control the supply of cocaine, with Bengal (1900), Bombay (1903), and Madras (1905) all introducing legislation attempting to restrict its sale to pharmacists and physicians. However, officials felt that, as an imported narcotic, the trade in cocaine would not be stemmed without international cooperation. India, then, had a genuine interest in controlling the cocaine trade—an ironic position given its role in the opium trade. Despite the rhetoric of the temperance movements, it appeared at the Hague that the Government of India was among those attempting real control of the trade in intoxicants.

With narcotics control built into the principles of the League of Nations, the controversy continued after 1918. Under pressure from the Home Office, the Viceroy of India announced in February 1926 that all remaining nonmedicinal exports of opium would be prohibited within a decade. As suspected by those involved, this simply resulted in the substitution of Turkish for Indian opium, rather than diminishing the availability of opium on the black market. Even worse was the fact that the substitutes were of a higher and more addictive quality than the Indian product had been. As such, the attempts to reduce India's role in the opium trade offered a template for many of the problems of international narcotics control since then.

Historically, opium was a major component of the South Asian colonial economy. It bolstered government revenues, brought bullion into the country, and provided India with a trade surplus with its Asian neighbors. It also provided the financial wherewithal underpinning the expansion of the British Empire in the region. Opium, ironically, which had nourished empire, also helped to undermine its foundations. Not only did it form part of the nationalist argument against the colonial rulers, it also divided them. The

debates over opium were a fundamental element in the gradual split between the British government in Whitehall and the British Government of India. However, the story of opium did not end with the end of empire.

MODERN PRODUCTION

In another of history's ironies, in the modern world India remains the largest producer of raw opium for the licit medicinal market. Not only does world consumption of morphine-based medications such as codeine continue to rise, Indian opium is also an excellent raw material for the new generation of thebaine-based opiates such as oxycodone (thebaine is an opiate alkaloid and a minor constituent of opium). India was designated one of only seven countries permitted to produce export grade opium for pharmaceuticals under the 1948 Paris Protocol, which, after much negotiation, formed the basis of the 1961 Single Convention on Narcotic Drugs. Pakistan, however, was only permitted to produce opium for domestic consumption and its government refused to sign the protocols. Apart from again upsetting the fragile regional political balance, there are serious concerns about the trade's control and the quantities of opium produced. Opium leaches from the licit into the illicit narcotics market because traffickers can pay significantly more than government buyers. At the same time, thebaine-based pharmaceutical products are being abused by drug addicts because of their stimulatory effects, re-creating the historical pattern of medicinal-to-illicit drug use.

In the modern narcotics trade, India and Pakistan continue to be geographically vulnerable. Whereas northeastern India increasingly serves as an outlet for the illicit opium and amphetamine products of the Golden Triangle (e.g., Southeast Asia), Pakistan has become the primary conduit for the narcotics smuggled out of the Golden Crescent (the drug-producing regions of Afghanistan, Iran, and Pakistan). Seventy percent of Afghanistan's poppies are grown in the provinces bordering Pakistan. This fact, combined with the civil strife and political corruption within Pakistan itself, has created the perfect conditions for the expansion of opium and heroin production in the region. The U.S. Central Intelligence Agency (CIA) has been charged with repeating its mistakes of the Vietnam era, with covert American operations in Afghanistan and Pakistan providing local warlords the wherewithal to link the region into the complex web of international narcotics criminals.

In South Asia, American geopolitics has once again come into conflict with the local governments and peoples through the U.S. desire to destroy narcotics traffic at its source. Just as America once attempted to reduce the subcontinent's role in the nineteenth century Chinese opium trade, its actions in the late twentieth century bolstered the narcotics trade of South Asia. Illicit raw opium production in Pakistan, which had been decreasing until the 1990s due to a relatively effective alternative development program, once again increased, and the region has also become the base for the manufacture of heroin from Afghan opium. It is assumed that the illicit laboratories are based in Pakistan because of easier access to supplies of acetic anhydride and other precursor chemicals required for the manufacture of heroin.

India has repeated this pattern. Political instability in its states that border Burma (Myanmar) has created the perfect condition for narcotics trafficking. International financial contributions to reduce the production and trafficking of opium in the subcontinent have increasingly come under the umbrella of the "war on drugs," and therefore fewer resources are focused on the alternative development of new cash crops. Instead, these resources are part of a frontline battle against local suppliers, including aid for helicopters and equipment for the Pakistan Anti-Narcotics Force. The battle is not going well. In 2005 the Pakistan authorities seized 24 metric tons of heroin and morphine products, which amounted to 27 percent of annual global seizures (United Nations, 2008).

The narcotics trade has resulted in several long-term consequences for the region. Authorities in both countries are concerned that the increased role in international distribution networks for illicit drugs has massively increased domestic consumption. Patterns of consumption have also changed from traditional forms to the more highly addictive practices of opium smoking and heroin injection, further increasing the number of addicts, which, in turn, has been linked to the high incidence of HIV/AIDS in South Asia. Attempts over the years by Indian and Pakistani anti-narcotics forces to coordinate their operations have been hampered by the

geopolitics of the Kashmir situation. Both countries also face the environmental fallout of cultivation, including land erosion and deforestation.

OTHER DRUGS

While government interest has been focused upon the opium and heroin trade, policies against other intoxicants have received a lower priority. There is evidence that suggests that cannabis consumption remains high, buoyed by relatively low prices and ease of production. The evidence also suggests that, as in the West, there has been increased abuse of amphetamines, benzodiazepines, and other synthetic intoxicants—an increase made easy by the proximity of India and Pakistan to Thailand. The control of the abuse of benzodiazepine and other pharmaceutical products is made more difficult by the fact that they are licit medicinal drugs.

Of course, not all the intoxicant problems of the subcontinent stem from consumption of illicit narcotics. The countries also have problems with licit intoxicants such as alcohol and nicotine. The 1950 constitution of the newly independent India enshrined the temperance ethos of Gandhi. The consumption of liquor, as well as tea and coffee, was regarded by many nationalists as an unwelcome infiltration of Western habits that altered long-established local patterns of consumption. It was also felt that this contributed to the cultural as well as political hegemony of the colonizers. However, most provinces ignored prohibition in practice, deriving some 20 percent of their taxable income from alcoholic beverages. This was a continuation of earlier ambivalent attitudes toward alcohol in the colonial period. While distilled beverages had long been part of social custom in the subcontinent, there were strong prohibitionist ethics within its major religions. Unlike government attitudes to opium and cannabis use, the *abkari* (excise) policies of the British colonial state toward alcohol had a strongly prohibitive stance, no doubt reflecting metropolitan attitudes toward alcohol consumption by the working classes as detrimental to their efficiency and morality, as well as raising the specter of racial degeneracy.

In South Asia, colonial officials viewed the unregulated distilling of alcohol as a potential source of social unrest and criminality, and they sought to restrict brewing to licensed premises only. Imported alcoholic beverages, including medicinal products, were also heavily taxed. However, *abkari* became a significant element in provincial state income, and increasing numbers of licenses were granted—alongside an increasingly sophisticated and expensive police operation against unlicensed liquor distilling. This unlicensed production has continued into the twenty-first century, with regular reports of fatalities and injuries caused by adulterated "country" liquor in both India and Pakistan.

TOBACCO

By the late nineteenth century, India was the largest producer of tobacco in Asia, and its output of 340 million pounds was four-fifths that of the American harvest. However, the bulk of India tobacco at this time was retained for the domestic market, augmented by significant imports of British manufactured cigarettes (Goodman, 1993). The smoking of cigarettes and *bidis* (roll-ups) in India has had a significant long-term impact upon its population. According to the World Health Organization, 12 percent of the world's smokers are to be found in India, and it remains one of the few countries in which cigarette consumption continues to grow. This has resulted in high levels of mortality and morbidity from smoking-related cancers and cardiac and respiratory disease. For instance, India has the world's highest incidence of oral cancers, and its high tuberculosis rates have also been associated with smoking.

As the price of cigarettes has tumbled in the region, the consumption levels soared. A 2008 report on smoking in India suggests that the problem is serious, with one in five children in India using some form of tobacco regularly. The report estimates that 20 percent of deaths in men aged 30 to 69 result from a smoking-related illness, and it predicts that smoking will result in around 1 million deaths annually (Jha et al., 2008).

India has banned smoking in public places, but with India having been a major exporter of cigarettes since the 1970s, it remains to be seen if there will be a more sustained campaign against smoking. Tobacco is also grown in the North-West Frontier Province of Pakistan, and there are fears that exploitation by the large cigarette manufacturers pushes cultivators into poppy production. Cigarette smuggling from throughout Asia into Pakistan is also a major

problem, and the health problems linked to smoking are increasing, just as they are in India.

In South Asia, as is the case elsewhere in the world, the distinction between illicit intoxicants and the licit products of tobacco and alcohol will require a major change in public perception of the dangers of smoking and drinking before any long-term change in habits is possible. Intoxicants, both licit and illicit, continue to play a major role in the lives of the peoples of India and Pakistan, and it remains to be seen how effective the recent internationally backed public health and anti-narcotics policies of the two nations will prove to be.

See also **Afghanistan; Alcohol: History of Drinking (International); China; Coca/Cocaine, International; Foreign Policy and Drugs, United States; Golden Triangle as Drug Source; Hashish; International Control Policies; International Drug Supply Systems; Marijuana (Cannabis); Middle East; Opiates/Opioids; Opium: International Overview; Oxycodone; Religion and Drug Use; Substance Abuse and AIDS; Tobacco: An International Overview.**

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PATRICIA BARTON

INDUSTRY AND WORKPLACE, DRUG USE IN.

The drugs that have the most impact on the U.S. workforce are marijuana and cocaine, although heroin and illicit prescription-drug use also pose a significant risk. Besides impacting productivity, these drugs affect workplace safety because they may reduce an individual's reaction time, impair judgment and memory, promote aggression, and further a worker's delusions of performance capability. Their use also impacts workplace morale because of attendance and coworker relationship problems.

In 2004 and 2005, over 8 percent of full-time U.S. workers aged 18 to 64 regularly used illicit drugs. Workers in food service and accommodations, construction, entertainment and recreation, and mining had the highest rates, which exceeded 13 percent in these industries. Rates among part-time employees are also significantly higher, and men regularly use illicit drugs more often than women, although this gap narrowed between 1997 and 2007, according to the National Survey on Drug Use and Health.

SUBSTANCE USE BY EMPLOYMENT STATUS AND WORKER CHARACTERISTICS

Drug use among workers impacts the workplace in a variety of ways:

- Drug use lowers productivity. The George Washington University Medical Center reported in 2002 that problems related to alcohol and drug abuse cost American businesses over $134 billion

Industry categories	Percent
Accommodations and Food Services	16.9
Construction	13.7
Arts, Entertainment, and Recreation	11.6
Information	11.3
Mangement of Companies and Enterprises, Administrative, Support, Waste Management, and Remediation Services	10.9
Retail Trade	9.4
Other Services (Except Public Administration)	8.8
Wholesale Trade	8.5
Professional, Scientific, and Technical Services	8.0
Real Estate, Rental, and Leasing	7.5
Mining	7.3
Finance and Insurance	6.8
Manufacturing	6.5
Transportation and Warehousing	6.2
Agriculture, Forestry, Fishing and Hunting	6.2
Health Care and Social Assistance	6.1
Public Administration	4.1
Educational Services	4.0
Utilities	3.8

Table 1. Past month illicit drug use among full-time workers aged 18 to 64, by industry categories: 2002–2004 combined. (Source: Substance Abuse and Mental Health Services Administration, 2002, 2003, and 2004 National Survey on Drug Use and Health.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

in lost productivity annually, and that work performance drops significantly among those using drugs.

- Drug use causes accidents and injuries. According to the 1999 National Household Survey on Drug Abuse, employees who use drugs are over three times more likely to be involved in a workplace accident.
- Absenteeism and turnover are increased. A 1991 report by the National Association of Treatment Providers found that employees who regularly use drugs are absent from work more and change employers with greater frequency.
- Drug use increases an employer's medical costs. The National Institute on Drug Abuse reports that employees who use drugs cost their employers about twice as much in medical claims as employees who do not use drugs.
- Workers' compensation costs are increased. Nearly half of all workers' compensation claims are related to substance abuse, according to the National Council on Compensation Insurance (DWI Resource Center, 2008).
- Drug use promotes workplace theft and violence. James Reaves (1994) found that 80 percent of drug abusers steal from their workplaces to support their drug use, and a 1994 study by the Society of Human Resource Management found that substance abuse is the third leading cause of workplace violence.

EMPLOYER RESPONSE

Employers have implemented workplace drug-testing programs in an attempt to reduce these consequences. As a preventive measure in the workplace, drug testing had its beginnings in the Department of Defense, which initially used it to address the high addiction rates of soldiers returning from Vietnam in the 1970s. In 1981, after an aircraft accident on the USS *Nimitz* revealed drug use among the ship's crew, the Department of Defense launched an aggressive drug-testing program that included random testing.

Drug testing in the civilian workplace began in earnest in the late 1980s. It was driven at first by the nuclear power industry, which was concerned about the quality of construction of new plants and the safe operation of all nuclear plants. In 1988, the Nuclear Regulatory Commission (NRC) mandated random drug testing for all employees and contractors who had unescorted access within their licensed nuclear facilities.

In 1989 the United States Department of Transportation (DOT) mandated comprehensive drug-testing programs for all safety-sensitive personnel involved in the aviation, highway, railroad, mass transit, pipeline, and maritime industries, including robust random-testing programs. As of 2008, over 12 million workers were covered under these DOT programs. Many other civilian employers have implemented drug-testing programs, though most are limited to pre-employment and "for cause" testing.

In 1988, Congress passed the Drug-Free Workplace Act, which requires all federal grant recipients and federal contractors whose contracts exceed $25,000 to certify that they will provide a drug-free workplace, including awareness programs for employees and training for supervisors. However, there are no drug-testing requirements for employees. Today's drug-testing programs, whether mandated by the government or not, follow a time- and court-tested approach to ensure that an employer's obligation to maintain the health and safety of its workplace is

Employment status	Illicit drug use		Heavy alcohol use	
	Percent	Number in thousands	Percent	Number in thousands
Total	9.2	16,363	8.4	15,017
Full-Time	8.2	9,413	8.8	10,113
Part-Time	11.9	2,903	8.6	2,094
Unemployed	18.6	1,405	13.6	1,026
Other*	8.3	2,642	5.6	1,783

Table 2. Substance use by employment status and worker characteristics. Past month illicit drug use and heavy alcohol use among persons aged 18 to 64, by Employment Status: 2002–2004 combined. (Source: National Survey on Drug Use and Health, The NSDUH Report, U.S. Department of Health and Human Services, July 23, 2007.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

unhindered and that the rights of the individual are safeguarded.

Best practice drug-testing programs include the following elements:

- A written policy, distributed to all employees, that establishes the employer rules regarding drug use, possession, and sale while at work, as well as the penalties for violating these rules.
- A drug-testing program that includes pre-employment testing for all applicants; random, for cause, and post-accident testing for employees; and return-to-work and follow-up testing for those employees who have tested positive, completed employer-designated counseling or rehabilitation, and returned to work after the successful completion of either effort.
- A helping program that employees and their families can use if they voluntarily seek help for drug use or other related family problems. These services are mainly provided by employee assistance programs (EAPs) funded by the employer, but they may also include referral to community based counseling and treatment programs.

DRUG-TESTING METHODOLOGY

When people use drugs, including tobacco, the drugs are found in all parts of the body. The drugs (and their breakdown products, called metabolites) are excreted in the urine, laid down in growing hair, and found in sweat and oral fluids (saliva). The most common drug test is a urine test. Hair tests are also widely used, and sweat patches and oral swabs are increasingly used to detect drug use. The chemical tests used for each type of sample are the same, beginning with an immunoassay screening test and going on to a more sophisticated confirming test when necessary.

Urine testing is used exclusively in all federally mandated drug-testing programs (e.g., NRC, DOT). Most other workplace drug-testing programs also use urine testing. The period of time in which a drug remains in the body and can be successfully found by a drug test is called the "window of detection." Drugs are usually found in urine for one to three days after the most recent drug use. Marijuana can be detected for longer periods for people who smoke every day for weeks at a time, but urine tests are usually negative after a day or two for people who smoke marijuana only occasionally.

Hair testing is used by employers who want a wider window of detection. The collection of the specimen is much less invasive than urine, and it is much easier to collect. A standard hair sample is one and a half inches long. Since hair grows about one half inch a month, this length of hair has information about drug use over the prior 90 days.

Sweat and oral-fluid testing are less common in employer-directed workplace programs, although the technology continues to develop. Ease of use is a major factor for using oral fluids or sweat. These methodologies also negate the requirements for time-consuming and costly urine collection procedures. Sweat patches are often used to monitor drug abstinence over time. Sweat is tested by applying a patch to the skin, and drug use is detected over the period the patch is worn, usually from one to three weeks. Oral fluids are tested by taking a swab from a person's mouth. They generally detect drug use within the last day or two after

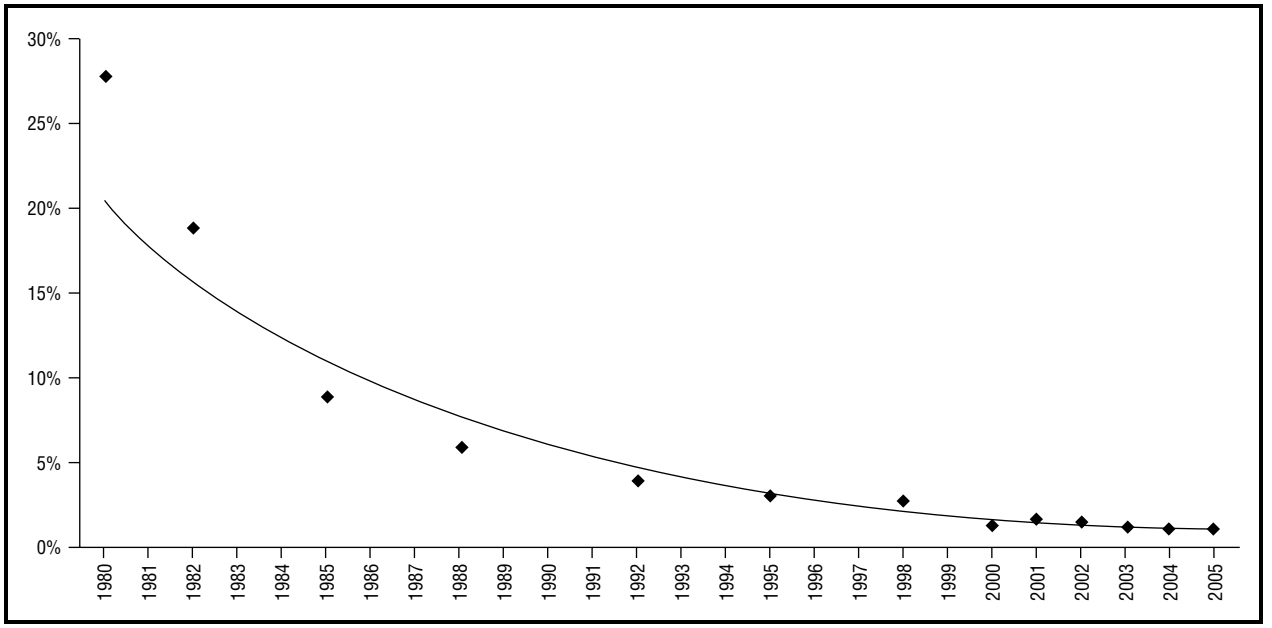

Figure 1. Active duty military drug positive rate, 1980–2005. (Source: Status of Drug Use in the Department of Defense Personnel, Fiscal Year 2005, Drug Testing Statistical Report, Office of the Deputy Assistant Secretary of Defense for Counternarcotics.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

the most recent drug use. Oral-fluid testing is often used in criminal justice and drug treatment programs, as well as the workplace.

THE TESTING PROCESS

The drug-testing programs themselves have three important elements: a controlled specimen-collection process, testing at a certified drug-testing laboratory, and a review of all tests by a medical review officer before the result is sent to the employer.

Collection efforts are designed to ensure that a collected specimen is not diluted, adulterated, or otherwise tampered with, while at the same time respecting the privacy and sensibilities of the donor. Well-developed specimen collection protocols are used by trained collectors, regardless of the methodology. The specimen protocols used for federally mandated drug-testing programs are outlined in the *Urine Specimen Collection Handbook for Federal Agency Workplace Drug Testing Programs* (2004), which is available online.

Analysis of the specimen is performed by certified laboratories. All drug tests performed under federally mandated programs must be tested at a laboratory certified by the National Laboratory Certification Program (NLCP), a program established and directed by the Department of Health and Human Services (DHHS). Laboratories will report out all test results only to a medical review officer. Drug tests that are conducted by employers but not mandated by the federal government will usually be analyzed at these certified laboratories, but they may be analyzed at laboratories certified by other credentialing agencies, such as the College of American Pathologists (CAP).

A medical review officer (MRO) is a physician who has been trained in the field of addictions. (According to the DHHS Medical Review Officer Manual for Federal Agency Workplace Drug Testing Programs, medical review officers must have the following background and credentials: knowledge about and clinical experience in controlled substance abuse disorders; detailed knowledge of alternative medical explanations for laboratory positive drug test results; knowledge about issues relating to adulterated and substituted specimens; and knowledge about possible medical causes for specimens reported as having an invalid result.) The MRO's primary duty is to determine whether there is a legitimate medical explanation for a laboratory positive test. If a laboratory test is positive, the MRO will contact the donor to discuss the results.

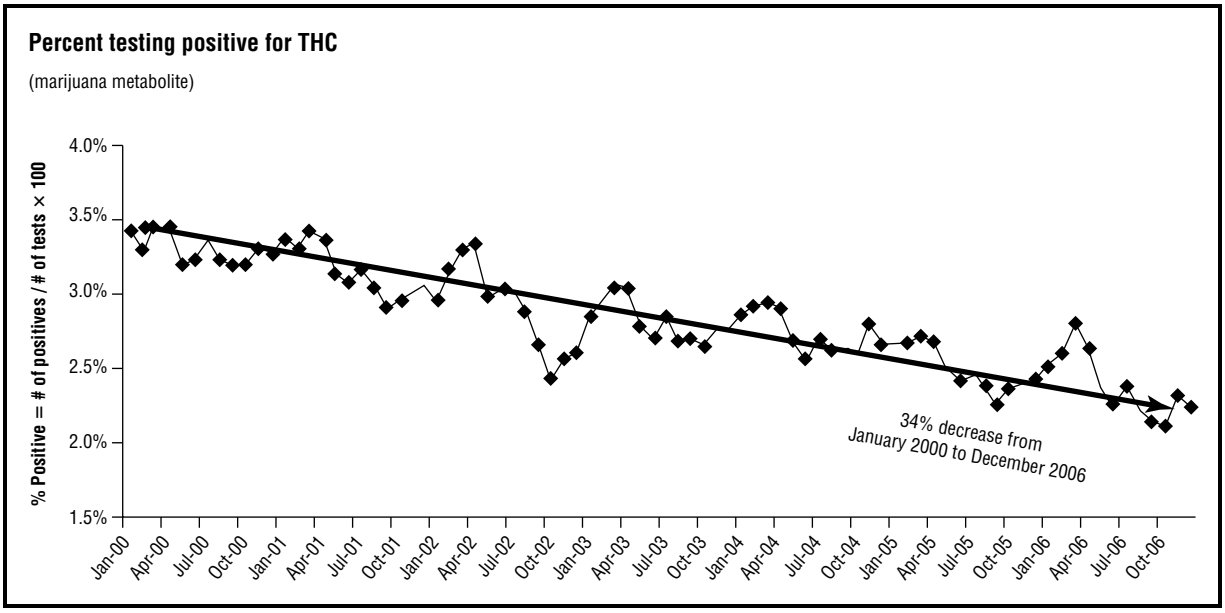

Figure 2. National workforce positives are down. (Source: Quest Diagnostics, through December 2006. Office of National Drug Control Policy, National Drug Control Strategy, 2008 Annual Report.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

In the discussion with the donor, the MRO will determine if the donor was using a properly prescribed drug that could have caused the laboratory positive result. If the MRO can verify the prescription with a pharmacist, physician, or dentist, the MRO will report the test as negative. If there is no verification, then the MRO will report the test as positive. Test results are sent to the employer by the MRO. The employer will usually receive an MRO report that says that the test was negative, positive, or invalid for a specific reason.

HELPING PROGRAMS

Comprehensive drug-free workplace programs usually include a helping component, which is designed to provide information, counseling, and other services for employees (and often for their families) who are having problems with drugs. Employee assistance programs (EAPs) are the most prevalent employer helping program. EAPs are intended to help employees deal with personal problems that might adversely impact their work performance, health, and well-being. They often include short-term counseling and referral services. Department of Transportation programs for the U.S. transportation industry also require that employees who have tested positive, in order to return to work, meet with a substance abuse professional, who will provide the employer with an assessment and a counseling or treatment regimen that must be completed before the employee can return to a safety sensitive job.

Other employees may provide information to employees regarding available community counseling and treatment programs, as well as other programs that are available. These programs may or may not be covered by the employee's health insurance. Twelve-step programs are often a viable option. Enrollment in employee assistance programs has risen steadily. In 1993, there were 27.2 million individuals enrolled in EAP programs, and by 2002 there were 80.2 million, representing a 194 percent increase since 1993 (Open Minds, 2002).

THE IMPACT OF DRUG TESTING

The results, where reported, are notable. For example, before the military began drug testing in 1981, its surveys indicated that over 25 percent of active duty military were regularly using illegal drugs. However, in a 2005 Department of Defense survey, the last one comparable with the 1980 data, that number was only 3.4 percent. Within DOT programs, the Federal Railroad Administration reports that the occupational injury rate among railroad workers was halved in the ten years following

the implementation of random drug testing in January 1990. Finally, a prominent index of national workplace drug testing has reported that the positive rate in the overall U.S. workforce decreased from 18.1 percent in 1987 to 4.1 percent in 2006 and that the positive rate for marijuana, the most widely used illegal drug, decreased by over one-third between 2000 and 2006 (Quest Diagnostics, 2007).

As reported by the White House Office of National Drug Policy, "[l]arger workforces were far more likely to have incorporated a comprehensive drug-free workplace program which has resulted in approximately 50 percent lower positive drug test rates, and 75 percent fewer self-reports of current drug use among workers compared to smaller worksites."

CONCLUSION

Substance use in the workplace negatively affects U.S. industry through lost productivity, workplace accidents and injuries, employee absenteeism, low morale, and increased illness. The loss to U.S. companies due to employees' alcohol and drug use and related problems is estimated at billions of dollars per year. Research shows that the rate of substance use varies by occupation and industry. Employers have responded by establishing drug-free workplace programs that include comprehensive drug-testing programs. Credible drug testing requires protocols that insure the rights of the individual while protecting the employers' rights to provide a safe and healthful workplace. Workplace-based employee assistance programs (EAPs) and community programs can be valuable resources for obtaining help for substance-using workers.

See also **Accidents and Injuries from Drugs; Drug Metabolism; Hair Analysis as a Test for Drug Use; Prevention.**

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RICHARD H. BUCHER

INFANTS EXPOSED TO ALCOHOL AND DRUGS.

See **Alcohol and Drug Exposed Infants.**

INHALANTS.

Inhalants are volatile solvents or anesthetics that are subject to abuse by inhalation. Most are central nervous system (CNS)

depressants, but some are convulsants. As a class they are characterized by high vapor pressure and significant solubility in fat at room temperature. Vapors and gases have been inhaled since ancient times for religious or other purposes, as at the oracle at Delphi in Greece. Experimentation with inhalants did not occur to any significant extent, however, until after the discovery of nitrous oxide and the search for volatile anesthetics commenced in earnest.

Arguably the most toxic and least studied among abused substances, inhalants can produce a wide range of injuries, depending on the chemical constituents of the products inhaled. Many are very complex mixtures formulated for a specific purpose or are used because they are the least expensive alternative, or both. Thus, their purity and safety are in no way comparable with those achieved by pharmaceutical companies manufacturing medications for human consumption.

Teenager huffing inhalant from plastic bag. © James Marshall/Corbis.

METHOD OF USE AND EFFECT MECHANISM

Inhalants are typically abused by achieving a high airborne concentration of a substance and deliberately inhaling it. With solvents, doing so typically involves putting the solvent in a closed container or saturating a piece of cloth and inhaling through it. Compressed gases are sometimes released into balloons and inhaled; directly releasing these substances into the mouth may freeze the larynx, causing laryngospasm and death by asphyxiation. Once the chemical is inhaled, its uptake and duration of action are determined by its solubility in blood and brain and by the respiratory rate and cardiac output.

The mechanism of action of this class of agents is less well understood than those of other drugs and medications. As CNS depressants, they have been thought to exert their actions by dissolving in membranes and altering their function in a nonspecific way; the potency of these compounds is frequently related to their solubility in membranes. Many consider this relationship to better predict the access of the agent to the site of action and to be unrelated to the mechanism by which the solvents exert their effects. Solvents impair conduction in isolated nerves and affect nerves with smaller diameters first, which suggests that parts of the nervous system such as the cortex would be affected before systems consisting of large fibers. There is significant interest in the GABA receptor complex as the site of action of many of these compounds. Some findings indicate that the rewarding effects of inhalant abuse are mediated through the same brain neurotransmitter systems and anatomical areas as have been implicated in other forms of substance abuse.

TYPES OF INHALANTS

Alkanes. Alkanes are hydrocarbons of the general formula CnH2n+2. The potency of this family of straight-chain chemicals increases with the number of carbons. The smaller molecules (methane, ethane, butane, propane) are gases at room temperature; their deliberate inhalation can produce cardiac arrhythmias and sudden death. Pentane, hexane, and longer alkanes are liquids that become

progressively less volatile. Hexane can produce a devastating neurotoxicity. Alkanes are paraffins; cycloparaffins are rings without alternating double bonds; and alkylcycloparaffins have a short substituent on the ring. Alkylcycloparaffins such as methylcyclopentane and methylcyclohexane (hexahydrotoluene) are convulsants.

Amyl Nitrite. Amyl nitrite is a volatile, oily liquid with a sweet, banana-like odor. It is sold by prescription in glass ampules for the treatment of angina pectoris, chest pain caused by the narrowing of vessels supplying the heart, resulting in inadequate blood flow. When the glass ampules are broken, they pop; hence, they are sometimes called *poppers*. Amyl nitrite relaxes the vessels of the heart by relaxing the muscles of the veins as well as all other smooth muscles in the body. When the veins throughout the body dilate, blood pressure falls. Because a minimum blood pressure is required to maintain blood supply to vital organs such as the brain, a reflex protects the brain by increasing heart rate and blood flow. This produces a *rush* as the heart pounds, and there is a throbbing sensation in the head. Users also experience a warm flush as the blood accumulates near the skin because of the dilation of veins. Vision also may redden as the retinal vessels dilate. The user may faint if the heart cannot maintain blood flow to the brain. If fainting occurs, the user falls to the floor, and blood flows to the brain, restoring consciousness. Use in a situation in which it is impossible to become horizontal may result in brain damage.

The duration of action of the drug is very brief, and as the effect wears off, the user may experience headache, nausea, vomiting, and a chill. The drop in body temperature occurs because of the loss of heat when the veins dilate and the skin flushes. Use of the drug for prolonged periods, or swallowing the liquid, may produce fatal methemoglobinemia, a blood condition in which the blood is brown and cannot carry oxygen to the brain. The drug produces a thick, crusty brown rash if it is spilled on the skin and is irritating to the lungs. It is flammable and explosive. Volatile nitrites are converted to nitrosamines in the body, and most nitrosamines are potent cancer-causing chemicals. Volatile nitrites impair the function of the immune system. There is an association of the use of volatile nitrites with Kaposi's sarcoma, an AIDS-related skin cancer, but this may be a surrogate variable for other hazards associated with the frequency of high risk sexual behaviors. The physiology of sexual intercourse involves smooth muscle; the nitrites relax those muscles as well and so will affect sexual function.

The prescription requirement for amyl nitrite was eliminated in 1960, and its use became popular; in 1964 prescription requirements were reestablished. So-called designer nitrites, such as butyl and isobutyl nitrites, were then bottled and sold as room deodorizers with such names as RUSH and Locker Room, and Aroma of Men (so named because it smelled like a locker room). Since these products were not controlled substances or sold as medicines, they were once legal products but were subsequently removed from the market, only to return when the formulation of the products was changed to escape regulation, as cyclohexylnitrite was not captured by the legislation.

Anesthetics. Anesthetics are used in medicine to permit surgical procedures without pain or consciousness. They are of two types: local and general. A local anesthetic is usually injected near nerves to prevent pain in a limited area, such as a procaine injection to anesthetize a tooth. General anesthetics are administered to the whole body and depress the CNS to such an extent that major surgery can be performed without killing the patient from the shock resulting from procedures that otherwise would be unendurable. General anesthetics were developed in the mid-nineteenth century by doctors experimenting, usually on themselves, with the organic solvents available at the time. These experiments were sometimes done by groups of people who inhaled the vapors and described the effects or passed out. Later, careful experimental work identified volatile chemicals that are used to save lives by permitting surgery that would otherwise be impossible to perform and that have relatively low toxicity and are relatively safe to use in medical contexts.

Some anesthetics can be given by injection. Short-acting anesthetics are used for brief procedures in medicine and dentistry when inhalation anesthesia is inappropriate or difficult or for starting anesthesia before longer-acting agents are given to the patient. Drugs that have been used for this purpose include barbiturates such as sodium methohexital and sodium thiopental, and benzodiazepines such as midazolam. Fentanyl and related

opioid compounds are used for a longer duration of action. A dissociative anesthetic, ketamine, is used for treating burn patients and small children. These agents affect the brain in a more selective way than other anesthetics, so that there is more muscle tone and better circulation in the head and neck. A related veterinary drug, phencyclidine (PCP), has a longer duration of action; when given to humans, however, it has produced terrifying hallucinations upon recovery. It is subject to abuse.

Volatile Anesthetics. Volatile anesthetics induce unconsciousness and loss of reflexes. This CNS depression can be induced by a wide variety of different chemicals; agents used in clinical medicine are selected for reasons that include low toxicity, ease of maintaining and adjusting a given depth of anesthesia, and freedom from adverse effects upon recovery. Many compounds were examined in the search for modern anesthetic agents.

The depth of anesthesia depends on how much of the medication is present in the CNS. This, in turn, depends on how much is in the air that is inhaled, to what extent the anesthetic divides between air and blood, and between blood and brain. An agent that is highly insoluble in blood, such as nitrous oxide, achieves a plateau, or saturation, concentration rapidly. More soluble agents take a longer time to plateau and to be exhaled as well, so recovery from them takes longer. Nitrous oxide and cyclopropane have the same solubility in blood and take the same amount of time to come to a steady concentration in blood; cyclopropane is more soluble in brain and fat, however, so it takes a much lower concentration to achieve the same effect. (Cyclopropane is explosive and, therefore, is no longer used in the operating room.) The way an anesthetic functions in a given individual depends on a number of variables, including the amount of fat in the individual's body, the volume of air inspired per minute, the amount of blood pumped through the lungs per minute, and various pre-existing medical conditions.

Aromatic Hydrocarbon Solvents. Aromatic hydrocarbon solvents have a structure that includes a benzene ring. The simplest form is benzene, a six-membered ring with double bonds and six hydrogen atoms. All other aromatic hydrocarbons have alkyl substituents around the ring; for example, toluene has one methyl group and xylene has two methyl groups.

Benzene. Benzene is a volatile aromatic hydrocarbon. Its presence in consumer products and in the workplace has been reduced because it causes a form of leukemia. Its chemical formula is C_6H_6; it is a six-membered ring with alternating double bonds and a hydrogen on each carbon. The ring opens when metabolized, causing the formation of reactive and toxic chemicals. Benzine, a name applied to automotive fuel in Europe, is a solvent mixture and should be distinguished from benzene.

Black Jack. Black Jack is the trade name for several inhalant products that contain either volatile nitrites or ethyl chloride.

Chlorinated Hydrocarbons. These substances comprise a large class of industrial chemicals. Those that are highly volatile are sometimes subject to abuse. Chlorinated hydrocarbons undergo significant metabolism in the body, and these changes in chemical structure usually result in an increase in the solvent's toxicity. Because many of these metabolic products are reactive chemicals, they can produce injuries to the kidneys, the liver, and the blood-forming organs. Chlorinated hydrocarbon inhalation is also associated with lethal disorders of heart rhythm, that is, ventricular arrhythmias.

Chlorofluorocarbon Propellants. Halogenated hydrocarbons are relatively non-reactive chemicals with high vapor pressure that have been used to blow products out of containers through a tiny hole. Their widespread use in the early 1960s was followed by an epidemic of aerosol sniffing that led to cardiac arrhythmias and death among young people. The halogens—chlorine, fluorine, and bromine—have been used to make various chemicals for purposes ranging from propellants and refrigerants to fire extinguishers. Their use has been severely limited since the recognition that their release into the atmosphere depletes the upper layers of ozone, exposing the Earth to excessive amounts of ultraviolet radiation. Freon is a brand name for a family of commercial products.

Chloroform. Chloroform ($CHCl_3$) was one of the earliest solvents put to use as an anesthetic agent, and it was widely abused in the nineteenth century.

It has been replaced with agents that are much less toxic. Its use in cough and cold medications is obsolete.

Ethyl Chloride. Ethyl chloride is a local anesthetic, CNS depressant, and refrigerant that has been subject to abuse by inhalation. Ethyl chloride has a high vapor pressure; spraying it directly into the mouth may freeze the tissues of the throat and cause fatal laryngospasm (contraction of the muscles of the throat and larynx), and the shutoff of the flow of air to the lungs. Ethyl chloride has been sold in canisters and spray cans (e.g., Black Jack). A related chemical, methyl chloride, has similar effects and was used in refrigerators until it was recognized as highly poisonous in closed spaces.

Ethyl Ether. A volatile anesthetic agent subject to abuse by inhalation, ethyl ether was used as an inhalation anesthetic for many years. It has been supplanted by other agents with fewer recovery side effects, such as headache, nausea, and vomiting. It is explosive. Ethyl ether was drunk during the Whiskey Rebellion of the eighteenth century, when heavy taxes were imposed on whiskey. Consumed by this route, ether *tanned* (hardened dramatically) the soft palate. When swallowed, profound intoxication follows, but recovery is faster than from alcohol. Alcohol is metabolized at a fixed number of grams per hour, except under extreme conditions; ethyl ether is eliminated by exhalation.

Freon. Freon is a brand name applied to a class of aerosol propellants commonly used as refrigerants. The availability of Freon has been limited since the 1990s due to increased recognition that chlorofluorocarbons and hydrochlorofluorocarbons negatively impact the Earth's ozone. Deliberate inhalation has been associated with sudden death from cardiac rhythm disturbances.

Gasoline. Gasoline, a fuel that powers internal combustion engines, is a complex petroleum product subject to abuse by inhalation. The toxicity produced from gasoline exposure depends on the constituents of the mixture and the route of administration. Oral ingestion of gasoline is usually followed by vomiting; subsequent aspiration of gasoline liquid into the lungs is followed by a frequently fatal chemical pneumonia. Deliberate inhalation of leaded gasoline fumes can lead to brain injury related to absorption of tetraethyl lead, a very toxic chemical.

Glue. Glues are made by dissolving a sticky or adhesive material in a solvent. When the solvent evaporates, the adhesive material remains attached to the surfaces to which it is applied, sticking them together. Glues are complex mixtures formulated for specific purposes. They are not designed for human consumption. When inhaled, they may produce severe injury or death. Most of the solvents used in glues are flammable, and fires have resulted from their inappropriate use. The solvent mixtures in glues and glue thinners are designed to dissolve the solid glue material and to evaporate evenly at a rate appropriate for the product. Solvents of relatively low industrial purity are used in these products; they are usually complex mixtures whose formulation changes with market price. Their toxicity can be great when concentrated and inhaled. Some manufacturers label their products or add irritants in an attempt to prevent youths from deliberately inhaling these products.

Hexane. Hexane is a volatile solvent that contains six carbons in a straight chain (i.e., an alkane) and has the chemical formula C_6H_{14}. It can cause severe damage to the peripheral nervous system, producing destruction of long myelinated nerves (distal axonopathy). This condition results in an inability to walk, loss of muscle mass in all limbs, and sometimes loss of bowel and bladder control. This injury occurs because hexane is metabolized to a gamma diketone. Another solvent subject to abuse that undergoes the same change in the body is methylbutylketone.

Nitrous Oxide. Nitrous oxide is a volatile analgesic and anesthetic agent. It was discovered at the beginning of the nineteenth century by Sir Humphry Davy, who was looking for gases and vapors that might have some therapeutic use. It is also used to increase the power output of engines, especially in race cars. Nitrous oxide quickly produces an inebriation that many found pleasurable, and it rapidly became the subject of much experimentation and merrymaking, which is why it is sometimes referred to as *laughing gas*. Nitrous oxide parties became very fashionable but could not long be limited to the upper classes. Popular

demonstrations were conducted, and at one such demonstration Horace Wells noticed that a participant had injured his leg, yet seemed oblivious to the pain. Although Davy had noted that nitrous oxide deadened the pain of his toothaches, it was Wells who underwent the first tooth extraction using nitrous oxide for pain relief. The first use of nitrous oxide for clinically significant pain relief was its use in childbirth by the physician Stanislav Klikovich (1853–1910). Nitrous oxide inhalation is about as effective as 30 mg of morphine for pain relief.

Nitrous oxide is not very soluble in either blood or brain tissue, and consequently it has a short duration of action and requires very high levels to produce effects, on the order of 15 to 30 percent by volume. Because the use of gases at this high a concentration might result in asphyxiation, special equipment is used to guard against this possibility in medical settings. Because it displaces oxygen, nitrous oxide can kill those who inhale it for pleasure in closed rooms or automobiles.

Nitrous oxide was long thought to be a relatively innocuous anesthetic, almost as safe as inert gases. Research has demonstrated, however, that its inhalation irreversibly inactivates methionine synthetase, and this enzyme inhibition produces a vitamin deficiency that can injure the peripheral nervous system. This was first observed in dentists and others with access to nitrous oxide who inhaled it habitually. This nervous system injury is associated with numbness and clumsiness of the hands and with Lhermitte's sign, a lightning-like shooting sensation that occurs when the patient bends the neck.

Nitrous oxide is used in dentistry because it has both analgesic and anxiety-relieving properties. It is used as a carrier gas and inducing agent in major surgery, facilitating induction of anesthesia maintained by other agents. Given that it is not very soluble in blood, oxygen must be provided to patients at the end of the surgery because the nitrous oxide can displace oxygen as it rushes out of the patient's body (diffusion hypoxia).

Perchloroethylene. This chlorinated hydrocarbon solvent, which was used in the dry-cleaning industry, is also known as PERC (see Chlorinated Hydrocarbons, above).

Toluene. Toluene (methyl benzene, toluol) is an aromatic hydrocarbon solvent widely used in industrial processes, fuels, and consumer products. It is among the least irritating of the aromatic hydrocarbon solvents. When inhaled, it can produce CNS depression, like alcohol and other solvents. Its pharmacologic effects resemble those of other CNS depressant drugs, displaying actions like those of medications used for the treatment of epilepsy or for the clinical management of anxiety.

Toluene is removed from the body by exhalation and by metabolism. It is metabolized to methylhippuric acid and is excreted by the kidneys. Overexposure to toluene can produce distal tubular acidosis of the kidney, an injury attributable to excess acidity that is reversible upon termination of exposure. Toluene has been demonstrated to produce loss of high-frequency hearing in laboratory animals following repeated high exposure, such as occurs during solvent abuse. Toluene also has been implicated in severe injuries to the nervous system in a large number of patients who deliberately inhaled toluene-containing solvents. These injuries are characterized by injury and loss of brain tissue. Patients display flattened emotional responses, impaired cognitive abilities, and a wide, shuffling gait associated with injury to the cerebellum. As of 2008, animal studies had not conclusively demonstrated that toluene alone is responsible for this severe brain injury syndrome; nonetheless, solvent abusers who inhale toluene-containing mixtures run a very high risk of irreversible brain injury.

1,1,1 Trichloroethane (TCE). This chlorinated hydrocarbon solvent has a high vapor pressure. It is useful in products that need to dry quickly, such as liquid paper products once commonly used to cover errors. The deliberate inhalation of these products has been associated with sudden death from ventricular arrhythmias (see Chlorinated Hydrocarbons, above).

Trichloroethylene. A chlorinated hydrocarbon solvent used as a degreaser and dry-cleaning agent, trichloroethylene is subject to abuse by inhalation. When alcohol is consumed after exposure to trichloroethylene, profound blushing of the face occurs, the so-called degreaser's flush. One of the metabolites of trichloroethylene is chloral hydrate,

an anesthetic agent used in a Mickey Finn, a spiked drink used criminally to anesthetize robbery victims.

Whippets. Whippets are small canisters of nitrous oxide used at soda fountains to make whipped cream. They have been incorporated into various products, such as balloon inflators, carburetor pipes, and other drug paraphernalia (see Nitrous Oxide, above).

See also **Inhalants: Extent of Use and Complications; Monitoring the Future.**

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INHALANTS: EXTENT OF USE AND COMPLICATIONS.

Inhalant abuse first became prevalent in the United States in the 1850s and is in the early twenty-first century endemic among adolescents. One of the most common forms of substance abuse, it is aptly referred to as the *silent epidemic*. Inhalants are also one of the most understudied types of substances. Commonly abused inhalants include acetone, butanone, n-hexane, and toluene, although varied mixtures of chemicals are found in many abused products. Intoxication presents as a general syndrome marked by slurred speech, ataxia, stupor or coma, and other signs similar to alcohol intoxication. Inhalant abusers may inhale vapors from a rag soaked with a substance placed over the mouth or nose, a bag into which a substance has been placed, or directly from a container. Intoxication is rapid in onset and short-lived, although some users repeatedly administer inhalants to maintain a preferred level of intoxication.

The *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*) distinguishes inhalant use disorders (i.e., disorders caused by the inhalation of aliphatic, aromatic, and halogenated hydrocarbons, as well as esters, ketones, and glycols) from disorders related to the abuse of anesthetic gases (e.g., nitrous oxide) or short-acting vasodilators such as amyl or butyl nitrite. Unlike other substance use disorders, withdrawal symptoms are not a criterion used for defining inhalant dependence in *DSM-IV*.

PREVALENCE AND CORRELATES OF INHALANT USE

Results from the 2006 Monitoring the Future (MTF) survey indicated that approximately 16.1 percent of eighth graders reported lifetime inhalant use. This rate of use was slightly higher than the comparable rate of marijuana use (15.7%) and substantially higher than the lifetime prevalence of cocaine use (3.4%) among this age group. Results from the National Survey on Drug Use and Health (NSDUH, 2002–2004) showed that an average of 598,000 youth twelve to seventeen years of age reported initiating inhalant use in the year prior to being surveyed. The NSDUH data also revealed that trends in past year inhalant use among this age group remained stable for males between 2002 and 2005. However, the prevalence of use increased from 4.1 percent to 4.9 percent for girls over this period.

Recreational inhalant use progresses to serious involvement with inhalants for many youth. For example, findings from the National Comorbidity Survey indicated that nearly 8.0 percent of youth fifteen to twenty-four years of age who tried inhalants eventually met *DSM-III-R* criteria for inhalant dependence. Inhalant use is found at epidemic levels in juvenile justice populations, with some estimates as high as approximately 40.0 percent (Howard et al., 2007). While inhalant use appears to be less prevalent among adults, it is important to note that it is problematic among disenfranchised adult populations, such as Native Americans who live on reservations, convicts, and other persons of low socio-economic status.

Asthma inhalers are typically not considered to be a substance of abuse. However, one study involving adolescents in the juvenile justice system found that approximately one-third of the sample had used an asthma inhaler without a prescription. Among youth with an inhaler prescription, approximately 27 percent reported using the inhaler more than prescribed (Perron & Howard, 2008). Coupled with other cases of inhaler misuse and abuse/dependence that are reported in the medical literature, it is likely that misuse and abuse of asthma inhalers is a greater problem than previously considered to be.

CONSEQUENCES OF INHALANT USE

Medical Consequences. Recreational inhalant use results in chemical exposures at levels dramatically higher than those typical of toxic occupational

exposures. Inhalant intoxication can lead to emergencies, including sudden sniffing death and serious accidents. Recurrent inhalant intoxication is associated with conditions, including Parkinsonism and other brain, liver, and kidney disorders. Neurological findings in inhalant abusers include cerebral atrophy, thinning of the corpus callosum, and lesions of the white matter. Brain imaging studies (e.g., fMRI and SPECT) indicate that regional decrements in cerebral blood flow can be observed after one year of inhalant abuse, whereas white matter changes may take years to develop (Okada et al., 2000). Such studies have found inhalant abusers to exhibit hypoperfusion foci and nonhomogeneous uptake of radiopharmaceuticals (Kucuk et al., 2000).

Legal and Social Consequences. Use of inhalants is associated with a wide range of adverse legal and social consequences. Inhalant users have higher rates of aggressive behavior, criminal offending, school problems, conduct disorder, substance abuse, and involvement in high-risk behaviors (including unprotected casual sex and IV-drug use) than other drug users/nonusers. Inhalant users in juvenile justice settings are more likely to commit a crime while intoxicated, sell drugs, or steal to acquire money with which to buy drugs than their inhalant-nonusing peers. Research on juvenile offenders has also revealed a wide variety of deleterious consequences attributable to inhalant use, including fistfights, property crime, and failure to meet social and vocational obligations.

Cognitive Consequences. Studies of occupationally exposed workers form the basis of much of what is known about cognitive deficits in inhalant-exposed persons (Hoek et al., 2000). Inhalant-related cognitive problems are slow to resolve in many patients, and even a single occupational exposure leading to inhalant intoxication can produce long-term memory problems and processing speed impairments (Stolley, 1996). This finding is ominous given that inhalant abuse is often characterized by repeated exposures to neurotoxins at levels that greatly exceed those of occupational exposures. The most common deficits found in this line of research include learning problems, auditory and visual abnormalities, memory and attentional deficits, and errors in recall and judgment. Cognitive impairment may be the most disabling consequence of inhalant abuse and the earliest sign of neurological damage.

Psychiatric Dysfunction. Inhalant users display high rates of multiple-drug use and conduct disorder as youth and substance dependence and antisocial personality disorder in adulthood. Inhalant users tend to exhibit an earlier onset of behavior problems and greater diversity in antisocial conduct than non-inhalant abusers. Prior reports have identified higher rates of mood disorders, particularly major depression, in inhalant exposed workers than controls. For example, journeyman painters were significantly more likely than controls (41.0% vs. 16.0%) to meet lifetime *DSM-IV* criteria for major depression, and eleven of twelve painters who met criteria for a mood disorder experienced their first episode of mood disorder after they had commenced their painting careers (Condray et al., 2000). Various studies also show an association of inhalant use with suicidal ideation, suicide attempts, paranoia, psychosis, impulse control disorders, and anxiety disorders among antisocial youth and other adolescent populations.

An important gap in the research is on the temporal ordering of psychiatric dysfunction and inhalant use. Specifically, it is unknown whether inhalants are used to alleviate psychiatric dysfunction (i.e., self-medication hypothesis) or if inhalants cause or exacerbate psychiatric dysfunction (i.e., super-sensitivity hypothesis). Most likely, there are heterogenous causal mechanisms within the population of inhalant abusers. A reciprocal relationship is probably at play.

TREATMENT AND PREVENTION

Research on treatment and prevention of inhalant use and abuse remained undeveloped in the first decade of the twenty-first century. As of 2008, no clinical trial of inhalant treatment had ever been funded by the National Institute of Drug Abuse, and no freestanding treatment facilities specializing in inhalant treatment existed in the United States. Moreover, inhalants are very rarely screened for in the United States, even within the substance abuse treatment service delivery system. Significant efforts are needed to effectively and efficiently identify persons who use inhalants. The identification of characteristic patterns of early cognitive dysfunction in inhalant users would contribute to future efforts to prevent inhalant-related brain damage. Psychiatric and substance abuse treatment providers should have knowledge about inhalants,

including risk factors for, and consequences of, inhalant abuse. Despite the absence of empirically supported treatments for inhalant use disorders, this knowledge can be beneficial in structuring treatment modalities to meet individual needs.

The most successful treatment approaches would likely focus on issues of psychosocial functioning. Attention would be directed toward social influences related to use, including identifying and avoiding risky situations, developing skills to manage peer influence, building social networks that do not include inhalant users, and creating opportunities for meaningful social engagement.

Prior research involving youth in the juvenile justice system indicate that adolescents used inhalants due to curiosity about their effects, feelings of boredom, ease of access, and enjoyment (Perron, Vaughn, & Howard, 2007). These reasons suggest that social marketing campaigns that heighten awareness of adverse consequences are needed to dispel myths that recreational inhalant use is an innocuous activity. Although current research shows that adolescents involved in the juvenile justice system are at elevated risk of inhalant use, further epidemiological research is needed in order to more effectively target social marketing campaigns. Other prevention efforts can occur with the manufacturing of substances that are commonly abused, such as changing formulas to reduce toxicity and adding irritants.

See also **Complications.**

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INJECTING DRUG USERS AND HIV.

One of the major risk behaviors for infection by the human immunodeficiency virus (HIV) is the multi-person use (sharing) of needles and syringes for injecting drugs; the other risk behavior is unprotected sexual intercourse with an HIV-infected partner. The National Institute on Drug Abuse (NIDA) estimated that there were between 1.1 and 1.3 million injecting drug users (IDUs) in the United States in the late 1980s (Centers for Disease Control, 1987). The number of injecting drug users has probably declined somewhat since then because fewer people are injecting, people are transitioning to non-injecting drug use, and more people are dying due to AIDS and other causes.

BACKGROUND

In 2006, 22 percent of the estimated 433,000 people in the United States living with the HIV infection reported injecting drug use as their primary risk, and an additional 3 percent reported both male-with-male sexual behavior and injecting drug use as risk. Injecting drug use has been declining as a route of HIV transmission in the United States (Santibanez et al., 2006) and in Western Europe (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2007) but has been increasing dramatically in Eastern Europe and Asia. Approximately one-third of new cases of HIV infection outside of sub-Saharan Africa are related to injecting drug use (UNAIDS, 2007).

Historically the most commonly injected drug has been heroin; however, the increased availability of cocaine has resulted in an increased use by IDUs since the late 1980s. Injecting cocaine has elevated the risk of spreading HIV because the shorter duration of a cocaine high leads to more frequent injecting (Gottlieb & Hutman, 1990), and the possibility that cocaine injectors may confuse whose syringe is whose in a session with multiple injections by each person.

The prevalence of HIV and AIDS among injectors varies widely from region to region in the United States. The highest rates of IDU and HIV are found along the East Coast and West Coast, in the Southwest, Florida, Puerto Rico, and in major metropolitan areas. The prevalence of HIV infection is also related to the social context of needle sharing. In areas where injectors go to *shooting galleries*—where anyone using a previously used needle may not know who else used the needle—there are generally high rates of HIV infection. Conversely, in areas where the IDUs share syringes within small social networks, transmission is likely to be much lower

While IDUs with HIV infection are predominantly Hispanic and African American men in their late 20s to mid-40s, variations and exceptions are noted and reflect dynamics in individual metropolitan areas. Historically, HIV prevalence among IDUs has been highest in the mid-Atlantic states (New York, New Jersey, Pennsylvania).

REDUCING RISK-TAKING BEHAVIOR

Drug-abuse treatment and prevention can be effective in controlling the spread of AIDS among IDUs and for reducing the risk of exposure to the HIV virus. The goal of treatment is to eliminate injecting drug use as a risk factor in the spread of HIV. The goal of prevention is to reduce and eliminate harmful behaviors, such as sharing needles, that place the IDU at risk for either becoming infected or infecting others with HIV. Prevention does not necessarily focus on changing drug-seeking and needle-using behavior. Four areas are considered to be of prime importance:

1. Increase the number of drug abusers in treatment;
2. Enhance the effect of treatment;
3. Develop outreach and counseling strategies;
4. Develop prevention strategies for reducing the risk-taking behavior among IDUs

Drug Treatment. Several organizations and groups have suggested that drug-abuse treatment is important in helping to decrease and prevent the spread of AIDS. These organizations include the World Health Organization (WHO); the American Medical Association (AMA); the National Academy of Sciences, Institute of Medicine; and the Presidential Commission on the HIV Epidemic.

Drug-abuse treatment can play an important role in preventing HIV transmission. Treatment reduces the number of people engaging in risky behavior. In addition to reducing the number of active drug addicts, treatment can also reduce the number of people recruiting new drug addicts (Brown, 1991). Barriers to treatment now exist for IDUs with HIV. The most serious barrier to drug-abuse treatment is the lack of treatment availability and programs.

Drug-abuse treatment incorporates several modalities, which include drug-free outpatient services, methadone maintenance programs, and therapeutic communities (Leukefeld, 1988), as well as a number of programs that do not fit into these categories. Ideally, HIV and drug treatment should be integrated to increase social support systems, which should increase adherence to medication schedules and resistance to drugs (Stein et al., 2000).

Outreach and Counseling. One way to increase the number of IDUs in treatment is to increase the number of outreach and counseling programs. The National AIDS Drug Abuse Research Demonstration Program is an example of outreach and counseling (National Institute on Drug Abuse, 1988). This demonstration program, initiated in 1987, provided an opportunity to assess the characteristics and risk-taking behaviors of injecting drug abusers not in treatment. Additional purposes included focusing on sexual partners of IDUs at high risk for AIDS, determining and monitoring HIV seroprevalence (rate that a given population tests positive) across cities, and evaluating prevention strategies. The overall goal was to reduce the spread of HIV infection by reducing and eliminating drug-use practices and certain high-risk sexual practices. Counseling and outreach approaches were applied, tested, and

evaluated at each community site. Projects were targeted on three levels: (a) high-risk individuals, (b) family and social networks of IDUs, and (c) the larger community. Although intervention components varied across sites, the focus and objectives were similar (McCoy et al., 1990; Leukefeld, 1988). These projects provided information about protective behaviors, and IDUs were encouraged to enroll in drug-abuse treatment programs. Trained indigenous outreach workers distributed and discussed materials through informal groups or through one-on-one interactions. Sixty-three communities were involved in this demonstration project (McCoy & Khoury, 1990; Leukefeld, 1988).

Strategies for community outreach differ between the IDU, their sex partners, and commercial sex workers. Reaching the IDU means that outreach workers go to places where IDUs hang out and buy their drugs, as well as visit jails, prisons, and courts, drug-treatment centers, and the health-care system. Although there is inherent danger in many of these settings, recovering drug users—savvy men and women of the same backgrounds as IDUs—have achieved success in contacting IDUs in these settings (Serrano, 1990; Brown, 1990).

Many male IDUs hang out on the street or can be found in places where other IDUs hang out. However, female sex partners of IDUs are often employed and frequently stay close to home with children. (Margolis, 1991). While women may purchase drugs for their partners, they do not generally hang out at those locations. Thus, targeting female partners of IDUs requires different strategies than those used for contacting the IDU.

The YES project of San Francisco is an example of a program that targeted female sex partners of IDUs. It began by supporting high-risk women in meeting their basic needs by helping them get general assistance, food, clothing, and health care. A second strategy was to rent a hotel room, called A Room of Her Own in which education and counseling was provided to the female partner of the IDU. Another project (serving Bridgeport, Connecticut; San Juan, Puerto Rico; and Juarez, Mexico) contacted the female sex partners of male IDUs. It examined an approach that attracted women to a safe setting established by the program—a clothing boutique where women could pick up new clothes and then stay to view an AIDS information video. Another strategy of this project was to have outreach staff available in the afternoons and evenings, hours when these women were available (Moini, 1991). There was also a project in Long Beach, California, where a drop-in center was established for youth and women (Yankovich, Archuleta, & Simental, 1991).

Commercial sex workers are another high-risk group and require strategies appropriate to their environment. Contacting commercial sex workers can be difficult because their pimps can severely restrict contact with social-service workers. In one study, contact was made when the pimp was not around and through the Salvation Army mobile canteen that served coffee to the sex workers in the late night and early morning hours (Moini, 1991). Another study reported that sex workers are aware of AIDS, know how it is transmitted, and are aware that their drug use and unsafe sexual behavior are putting them at risk (Shedlin, 1990). However, barriers to behavioral changes in commercial sex workers include low self-esteem and low levels of education, along with poverty, addiction, hopelessness, lack of knowledge, and lack of support services.

Prevention Strategies. Prevention is of central importance in controlling the spread of HIV among IDUs. Reducing syringe sharing among people who continue to inject drugs is the most important aspect of preventing HIV transmission among drug users. Preventing infection is a self-preservation issue, while preventing the spread of HIV is an altruistic issue (Moini, 1991). Reports have indicated that among IDUs there is greater resistance to changing sexual behaviors (using condoms) than drug-use behaviors (sharing needles) (Sorenson, 1990). Thus, it is important to target not only IDUs but also their sex partners and commercial sex workers who engage in unsafe sex practices. These people may also be exchanging drugs for sex and may be IDUs themselves (Centers for Disease Control, 1990a). There are three prevention strategies available:

1. Education
2. Needle-exchange programs
3. Community-based interventions

Education. In addition to the community-outreach programs, Jean Schensul and Margaret Week (1991) indicate that three overarching prevention-education strategies have been developed

1. Prevention education for HIV-antibody-negative individuals;
2. AIDS pre- and posttest counseling;
3. Prevention and support for HIV-antibody-positive individuals

AIDS prevention education involves delivery of information related to the spread of HIV, risk behaviors, and preventing the spread of the virus. Educational activities target the general public, school-aged populations, and populations at risk, like IDUs. The U.S. Centers for Disease Control (CDC) National Public Information Campaign produced numerous educational materials for the radio, television, and print media. Education targeting individuals at risk for HIV infection has included counseling, testing, teaching of behavioral responses to risky behaviors, and providing support for low- or no-risk behaviors (Roper, 1991).

Prevention education for IDUs includes several informational components. Of primary importance to active-drug users are issues related to needle sharing as a risk behavior for HIV transmission. Safe-sex issues and knowledge of HIV transmission through unsafe sex are important to IDUs, the sex partners of IDUs, and commercial sex workers.

Pre- and posttest AIDS counseling is another strategy for HIV prevention. In the early 1980s, at the beginning of the AIDS epidemic, testing was controversial because of the fear of discrimination, the concern about the accuracy of tests, the usefulness of the results, and the psychological distress associated with a positive result. However, because there is more effective treatment for symptomatic AIDS and early treatment for HIV-infected individuals, the resistance is diminishing.

Generally, individuals seek HIV testing for one of two reasons: (a) an agency or person (like a plasma center, a penal institution, or a medical professional) requests it, or (b) the individual seeks to be tested because of identified high-risk behaviors (Roggenburg et al., 1991). When an individual is tested for HIV, it can represent a crisis in the life of that individual. Receiving the results can be difficult due to the anxiety surrounding the situation, even if the results are negative. Pre- and posttest counseling are necessary to assess the psychological well-being of the individual being tested.

A very important approach for preventing HIV infection is providing legal access to sterile injection equipment for IDUs (Committee on the Prevention of HIV Infection among Injecting Drug Users in High Risk Countries, 2006). Access is provided through sales in pharmacies, needle exchange programs, or both. In needle exchange programs, a clean needle and sometimes injection equipment (works) are exchanged for used ones. Large-scale syringe exchange programs have been associated with both preventing HIV epidemics among IDUs (Des Jarlais et al., 1995) and reducing high seroprevalence epidemics (Des Jarlais et al., 2005). Syringe exchange started in the United States in the late 1980s, and there are now approximately 180 needle exchange programs in the United States (McKnight et al., 2007) and a number of states (Connecticut, New York, Minnesota) have changed their laws to permit pharmacies to sell sterile needles and syringes to drug users. While it is difficult to draw strict causal relationships, the number of HIV infections among injecting drug users in the United States has been declining substantially (McKnight et al., 2007) since the expansion of syringe exchange in the country.

FUTURE DIRECTIONS FOR PREVENTION AND TREATMENT

Preventing the spread of AIDS for IDUs and their sex partners requires a multidisciplinary, multiple-strategy approach. Community-intervention strategies have proven to be partially effective in reducing IDU risk behaviors. Much remains to be accomplished, however, particularly in low- and middle-income countries (Committee on the Prevention of HIV Infection among Injecting Drug Users in High Risk Countries, 2006). Targeting HIV-prevention approaches and interventions will receive additional emphasis as the epidemic progresses. Research needs to continue to examine methods to reduce HIV in IDUs, to reinforce IDU behavior changes, to increase the effectiveness of drug-abuse treatment, and to provide antiretroviral treatment with psychosocial support and other support systems for HIV-infected IDUs.

See also **Cocaine; Eastern Europe; Harm Reduction; Heroin; Hispanic Americans, Alcohol and Drug Use Among; HIV Risk Assessment Battery (RAB); National Survey on Drug Use and Health (NSDUH); Needle and Syringe Exchanges and HIV/AIDS; Prevention, Education and; Prisons and Jails, Drug Use and HIV/AIDS in; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Substance Abuse and AIDS; U.S. Government: Agencies Supporting Substance Abuse Prevention and Treatment.**

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INJURIES FROM ALCOHOL AND DRUGS.

See **Accidents and Injuries from Alcohol; Accidents and Injuries from Drugs.**

INTERNATIONAL CLASSIFICATION OF DISEASES (ICD).

International Classification of Diseases (ICD) is the official classification system of the World Health Organization (WHO), which is mandated to issue periodic revisions. As a general system for the classification of diseases, injuries, causes of death, and

related health problems, the ICD is used throughout the world as a frame of reference for statistical reporting of morbidity and mortality, clinical practice, and education. The ICD is a system of categories to which specific disease entities can be assigned consistently in different parts of the world. As of 2008, it has become the international standard of diagnostic classification for epidemiological and many health management purposes, including analysis of the general health situation of population groups and the monitoring of disease prevalence and incidence. It is used extensively to classify psychiatric disorders, including alcohol and drug dependence, and related health problems recorded on many types of health records, including death certificates and hospital reports.

Recognizing the growing importance of alcohol and drug misuse, the ninth revision of ICD published in 1975 (*ICD-9*) for the first time introduced the terms *dependence* and *abuse* into the international nomenclature. *Drug dependence* was defined as "a state, psychic and sometimes also physical, resulting from taking a drug, and characterized by behavioural and other responses that always include a compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effects, and sometimes to avoid the discomfort of its absence" (WHO, 1977, 1978, p. 42). *Alcohol dependence* was defined in a similar way. The category Non-Dependent Abuse of Drugs was designed for cases in which a person "has come under medical care because of the maladaptive effect of a drug on which he is not dependent and that he has taken on his own initiative to the detriment of his health or social functioning" (WHO, 1978, pp. 43–44).

In 1994, the tenth revision of ICD was introduced. *ICD-10* replaced *ICD-9* as the official classification system for international use (WHO, 1992b). Chapter V, which describes mental and behavioral conditions (WHO, 2007), includes a section for the classification of disorders based on ten kinds of psychoactive substances: alcohol, sedative-hypnotics, cannabis (marijuana), cocaine, other stimulants, opioids, hallucinogens, tobacco, volatile solvents, and multiple drugs. The major disorders associated with these substances are acute intoxication, harmful use, dependence syndrome, withdrawal state, amnesic syndrome, and psychotic disorders (WHO, 2007). The identification of the substance used may be made on the basis of an interview with the patient, laboratory analysis of blood or urine specimens, or other evidence (such as clinical signs and symptoms or reports from third parties).

Acute intoxication is a transient condition following the ingestion of alcohol or other psychoactive substances. It results in disturbances in consciousness, cognition, perception, mood, or behavior. According to *ICD-10*, psychoactive substances are capable of producing different types of effect at different dose levels. For example, alcohol may have stimulant effects at low doses, lead to agitation and aggression with increasing dose levels, and produce clear sedation at very high levels. The term *pathological intoxication* in *ICD-10* refers to the sudden onset of violent behavior that is not typical of the individual when sober. This sudden onset occurs very soon after amounts of alcohol are drunk that would not produce intoxication in most people.

A central feature of the *ICD-10* approach to substance-use disorders is the concept of a dependence syndrome, which is distinguished from disabilities caused by harmful substance use (Edwards, Arif, & Hodgson, 1981). The *dependence syndrome* is defined as "a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerances, and sometimes a physical withdrawal state" (WHO, 2007). A central characteristic of the dependence syndrome is the strong and persistent desire to take psychoactive drugs, alcohol, or tobacco. Another feature is the rapid reappearance of the syndrome soon after alcohol or drug use is resumed after a period of abstinence. A definite diagnosis of dependence is made only if three or more of the following have been experienced during the previous year: (1) a strong desire or sense of compulsion to take the substance; (2) difficulties in controlling substance-taking behavior in terms of its onset, termination, or levels of use; (3) a physiological withdrawal state; (4) evidence of tolerance; (5) progressive neglect of alternative pleasures or interests because of substance use; and (6) persisting with substance use despite clear evidence of overtly harmful consequences.

Harmful use, a new term introduced in *ICD-10* is a pattern of using one or more psychoactive substances that causes damage to health. The damage may be of two sorts: (1) physical (physiological), such as fatty liver, injuries associated with alcohol intoxication, or hepatitis from a contaminated needle used to inject drugs; or (2) mental (psychological), such as depression related to heavy drinking or drug use. Adverse social consequences often accompany substance use, but they are not in themselves sufficient to result in a diagnosis of harmful use.

A *withdrawal state* is a group of symptoms occurring on cessation or reduction of substance use after repeated and usually prolonged high-dose use of that substance. Onset and course of the withdrawal state are related to the type of substance and the dose being used immediately before abstinence. The withdrawal state may be complicated by convulsions.

Amnestic disorder refers to chronic impairment of recent memory induced by alcohol or other psychoactive substances. Disturbances of time sense and ordering of events are usually evident, as are difficulties in learning new material.

Psychotic disorder in the context of psychoactive substance use is a cluster of psychotic symptoms characterized by vivid hallucinations (typically auditory, but often in more than one sensory modality), misidentifications, delusions, ideas of reference (often of a paranoid or persecutory nature), psychomotor disturbances (excitement of stupor), and an abnormal affect, which may range from intense fear to ecstasy. The disorder typically resolves at least partially within one month and fully within six months.

Chapter 5 of *ICD-10* is available in several different versions. The *Clinical Descriptions and Diagnostic Guidelines* is intended for general clinical, educational, and service use (WHO, 2007). *Diagnostic Criteria for Research* is designed for use in scientific investigations and epidemiological studies. A shorter and simpler version of the classification is available for use by primary healthcare workers.

See also **Addiction: Concepts and Definitions; Alcoholism: Origin of the Term; Diagnostic and Statistical Manual (DSM); Models of Alcoholism and Drug Abuse.**

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INTERNATIONAL CONTROL POLICIES.

The international control of drugs, such as opium, coca, cannabis, alcohol, and tobacco, started at the end of the nineteenth century. Before these drugs came under international control, their global exchange had been ruled by free trade. In fact, many of the states shaping the international control system in the twentieth century had profited from the drug trade in the centuries before. The most evident example was the flourishing trade in opium between China and the British colony of India in the nineteenth century, which provided the British Empire with crucial revenues.

The shift from free drug trade to control was the result of economic and political changes. Industrialization and growing world trade were the bases for the expanding global use and production of substances such as alcohol, tobacco, and opium. In response to this expansion, social reformers gathered political momentum against the, in their eyes, immoral drug trade at the end of the nineteenth

century. In particular, Christian missionaries were among the first to pressure the British and U.S. governments to limit their involvement in the alcohol and opium trade. Bishop Charles Henry Brent, who had gained firsthand experience of opium smoking and trade in the U.S. colony of the Philippines, zealously advocated the international prohibition of dangerous drugs (McAllister, 2000).

Moral crusaders inspired by Brent also found support for their cause in new medical research, which highlighted the health risks of drug use. Although opium and alcohol-based remedies had been indispensable to the medical chest for centuries, at the end of the nineteenth century medical research started to portray opium, alcohol, and manufactured drugs, such as heroin and cocaine, as great risks to people's health. Growing medical consensus on the dangers of drugs aided the campaigns of social reformers (Courtwright, 2001).

Against this background the first international meetings were held to discuss the regulation of the trade in opium, particularly in China. The 1909 Shanghai Opium Commission was the first such meeting, having been initiated by the U.S. and Chinese governments and presided over by Bishop Brent himself. The aim of the conference was to prohibit nonmedical opium use and to stop state-sanctioned opium exports.

In contrast to Brent's moral position, the U.S. government favored opium trade restrictions because they offered the United States strategic advantages. By supporting drug control, the U.S. government gained inroads into the opium-dominated Chinese market and improved U.S.-Chinese relations by supporting a policy in China's interest. The United States also claimed the moral high ground without having to compromise its economic interests in Asia. In contrast, major drug producing and manufacturing countries strongly opposed U.S. policy, as it threatened their favorable position in the opium market. As a result of these divergent political interests, the Shanghai Commission and the subsequent Hague Opium Conference (1911–1912) had few tangible effects on the international control of the drug trade.

DRUG CONTROL AFTER WORLD WAR I

The major step toward an international control system for opium, coca, and cannabis only occurred after World War I had reshuffled global power relations. The strongest opponents and potential losers of international drug control, such as drug-manufacturing Germany and drug-producing Turkey, were forced into the system at the peace conferences following the war. In addition, the newly founded League of Nations, the predecessor of the United Nations (UN), provided a permanent institutional basis for the negotiation and coordination of international drug control.

The two most important treaties negotiated under the League were the 1925 International Opium Convention and the 1931 Convention for Limiting the Manufacture and Regulating the Distribution of Narcotic Drugs. The 1925 Convention obliged members to report national opium exports and imports to the League-based Permanent Central Opium Board. The board also oversaw restrictions on the trade in coca and cannabis. The 1931 Convention concentrated on manufactured drugs and established a system by which governments estimated the quantity of drugs they required for medical and scientific use. This convention also introduced a drug-scheduling system that classified drugs according to the danger(s) they posed to health. The predecessor of the World Health Organization (WHO) was involved in this scheduling mechanism. In general, these two conventions established a reporting, estimating, and scheduling system that remained the basis for all later drug treaties (McAllister, 2000).

This early international control system under the League was effective at reducing the legal world trade in opium, coca, and cannabis products. It was the first time in history that a prosperous global trade was shrunk by international cooperation (Courtwright, 2001). However, after World War II the illegal smuggling of drugs soon caught up with the declining legal trade. In response, new treaties were drafted to close loopholes and to devise stricter controls on the illegal side of the drug trade. Compared to the legal trade, international cooperation would remain unsuccessful at stopping the rise of illegal drug trafficking throughout the twentieth century.

POST–WORLD WAR II

After World War II the UN and its specialized bodies inherited the drug-control mandate of the

League. UN bodies such as the International Narcotics Control Board (INCB) and the WHO replaced their forerunners. Traditional focal points for international control, such as China and Turkey, were replaced by new countries, such as Afghanistan and Colombia. But as in the first half of the twentieth century, the preferences of powerful Western governments continued to dominate the formulation and implementation of international control policies. Western preference for a supply stop of opium, coca, and cannabis from producer countries has remained the guiding principle of UN drug control. The U.S. government also continued to use its diplomatic and economic powers to force this preference onto producer states.

The treaties negotiated under UN auspices reflect these political preferences. The treaties extended the scope of international drug control, in particular in the field of illegal trade, and consolidated the ideas introduced in the first three decades of the twentieth century. The 1961 Single Convention on Narcotic Drugs was the culmination of the international drug-control effort started at the beginning of the century. The treaty had the dual goals of ensuring adequate medical and scientific supply of opium, coca, and cannabis products, as well as limiting all other cultivation, manufacture, trade, and use by strengthening the established reporting, estimating, and scheduling system. The treaty has remained the principal and most universally accepted agreement on drug control.

Through its aims and mechanisms, the 1961 Convention prioritizes a clear set of ideas on drug control, which is worth highlighting. The foremost method prescribed to intervene in the drug market is through supply-dominated measures, such as export and import controls. The convention mentions drug demand measures but does not institutionalize a single binding mechanism in this field. The main focus of the treaty is to minimize drug production, manufacture, smuggling, and distribution rather than use.

Besides supply control, the treaty prioritizes the control of opium, coca, cannabis, and their derivates over other drugs. In fact, during negotiations on the 1961 Convention drugs such as synthetic amphetamines were intentionally excluded because Western pharmaceutical companies opposed their control. These substances appeared in subsequent, less stringent treaties. Drugs more socially accepted in Western states, such as alcohol and tobacco, were not even discussed during the course of drafting the 1961 Convention and other treaties. Therefore, the 1961 Convention and international legal framework prioritize the control of opium, coca, and cannabis products over other drugs (McAllister, 2000).

It is important to note that the 1961 Convention and related international agreements do not establish the total prohibition of heroin, cocaine, and cannabis use, although this is often claimed in official statements. The international control system regulates as well as prohibits drug use and trade. It regulates the medical and scientific use of controlled substances and prohibits any other use. The line between regulated medical and prohibited nonmedical use is open to states' own interpretation. For instance, it allowed the government of the United Kingdom to legalize the medical prescription of heroin to addicts, although this practice was illegal in other countries. This and similar interpretative spaces in the international framework offer governments a certain level of discretion when implementing the international treaties.

In general, even though this interpretative discretion leaves some space for national decisions on drug control, the 1961 Convention and other drug-control treaties are clear in their preference for the supply control of opium, coca, and cannabis. They purport these preferences not only through the supply-control-dominated language used in treaties but also through obligatory mechanisms, which are confined to the drug-supply side. In this sense, the treaties clearly reflect the powerful interests of the main drug consumer states in Europe and North America, which have attempted to shift the burden of control to producer states. In addition, interpretative discretion is often unfeasible for poorer states, which are more vulnerable to pro-prohibitionist pressures from the U.S. administration. For instance, Turkey was bullied into the international control system with the threats of U.S. economic sanctions in the 1950s and 1960s.

UNITED NATIONS TREATIES AFTER 1961

The treaties that followed the 1961 Convention confirmed its dominant ideas. The 1972 Protocol Amending the Single Convention on Narcotic Drugs

continued to focus on minimizing illegal supplies of opium, coca, and cannabis products and the 1971 Convention on Psychotropic Substances extended the 1961 approach to a greater variety of drugs.

The second major UN drug-control convention besides the Single Convention was negotiated in 1988. The UN Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances was a direct outcome of U.S. President Ronald Reagan's domestic and international war on drugs from the mid-1980s onward and the realization among other UN member states that the existing conventions were lagging behind the growing global trade in illegal drugs.

The 1988 Convention reaffirmed the dominant drug-control system of earlier treaties and strengthened the importance of criminal justice—that is, policing, prosecution, and imprisonment—as the major method of drug control. Its main goal was to increase police and legal cooperation in the field of supply control. As in the treaties before, discussion of such issues as demand control and health were absent from the treaty and international debates at the time. This fact prompted observers at the time to state that until the 1980s, "the history of national and international narcotics control can be written without reference to addicts or addiction" (Stein, 1985, p. 5).

Together, the 1961 and 1988 treaties are the principal pillars supporting the international drug-control system. Drug-control agreements made after 1988 have had less impact on the legal control framework. However, these post-1988 agreements are important as this period witnessed a shift toward a more balanced international drug control approach. In particular, drug-demand reduction became more central in debates about international drug control throughout the 1990s.

DEMAND REDUCTION AS AN INTERNATIONAL PRIORITY

The main international agreements that represent this shift were made in 1987 and 1998. The principal product of the 1987 International Conference on Drug Abuse and Illicit Traffic was the Comprehensive Multidisciplinary Outline of Future Activities in Drug Abuse Control (CMO), which consisted of four equally important parts: drug-supply control, illicit drug traffic, illicit drug demand, and drug user treatment. For the first time, the CMO elevated drug-demand control to the same level of importance as supply control. The CMO especially served the interests of poor drug-producing states, which had advocated an equal international focus on the different aspects of drug control. In particular, Latin American states had opposed the overemphasis on the supply control of cocaine and the international neglect of U.S. drug demand.

Latin American states were also crucial in pushing for the revision of the international drug-control system at a major drug-control meeting in 1998, the UN General Assembly Special Session on the World Drug Problem (UNGASS). The meeting reaffirmed the CMO's aims and sought to establish a more equal relationship not only between supply and demand efforts but also between rich and poor states and their respective responsibilities in solving the world drug problem. In addition, states participating in UNGASS agreed to commit to attaining a "significant and measurable" reduction of drug demand (Donnelly, 1989; Jelsma, 2003).

RECENT DEBATE

Coinciding with UNGASS in the 1990s were broader international policy debates over drug legalization and harm reduction. These debates were part of a backlash against the ineffectiveness of the international control system, which had led to no significant reduction in illegal drug consumption, production, and trade. On one hand, proponents of a personal-freedom-centered approach, such as U.S. economist Milton Friedman, proposed drug legalization as an alternative to the internationally dominant approach. Legalization was meant to be a return to unregulated drug trade. The legalized trade in drugs would lead to the disappearance of criminal drug industries, which had developed as a result of drug control. In this view, legalization would also make the ineffective and expensive drug enforcement bureaucracy redundant. Legalization proponents saw control as the major problem that needed to be abolished.

On the other hand, harm reduction approaches grew out of medical concerns over the spread of HIV/AIDS through injecting drug use. In response to these concerns, harm reduction proposed a focus on the reduction of major drug-related harms rather than a reduction of drug use per se. Among the many

practices advocated by harm reduction, needle-exchange programs aiming to prevent the spread of HIV/AIDS through shared syringes as well as a more balanced emphasis on demand and supply control were common (Courtwright, 2001). In general, harm reduction emphasized the underlying reason behind drug control, that is, the protection of individuals' and societies' health, which had been sidelined by international drug control.

In international political circles, legalization remained of marginal importance, unless it was used by conservatives to discredit policy reformers. Harm reduction was practiced in several European countries and therefore had some impact on the sidelines of international conferences and on the practical work of the UN. But harm reduction also never made its way into international policy documents because it was strongly opposed by the UN's major donor, the United States.

Overall, if seen from a legal perspective, these policy debates as well as UNGASS had limited effects on the international drug-control system and its supply-control bias. It did not introduce any new binding mechanisms and institutional responsibilities. Even rhetorically, supply control still dominates the international drug-control system. At UN drug-control meetings, the language of "drug war" and "drug scourge" continues to be used by a majority of state representatives. This language affirms the dominance of supply control, criminal justice, and policing and has little in common with demand reduction, prevention, and medical patient treatment (Room, 1999).

However, a slight shift has occurred, if just on the rhetorical and not on a legal level. Drug-demand control was not considered worth debating until the 1990s and only then became significant enough to be reflected in international policy statements, such as the CMO and at UNGASS. Harm reduction has also been discussed in UN studies on alternative drug control, such as the 1997 World Drug Report (Jelsma, 2003). This shift has not reached, and might never reach, a level where supply control and demand control are equally important in the international legal framework. Nonetheless, there was an important shift away from pure supply control to the prescription of a more balanced approach in the 1990s.

NEW CONTROLS ON TOBACCO AND ALCOHOL

Finally, although few international policy reforms have evolved in the field of opium, coca, and cannabis control during the last few decades, in large part due to U.S. opposition, the control of alcohol and tobacco has seen new initiatives since the late 1990s. International measures to control tobacco gained new impetus after 1999, when the WHO began preparing a Framework Convention on Tobacco Control. That convention was adopted in 2003 and proposes restrictive sales measures, labeling requirements, protection from exposure to tobacco smoke, as well as measures against the smuggling of cigarettes. The treaty is most stringent in the field of advertising, although none of its provisions amount to the type of obligations existent in the field of opium, coca, and cannabis control. As the convention is primarily a framework for future legal developments, it remains to be seen how far international tobacco control will emulate the control of illegal drugs.

Nonetheless, international tobacco controls go much further than control measures for the world's most widespread legal drug, alcohol. International alcohol control has its historical precedents in alcohol prohibition in the Islamic world, as well as in treaties on liquor trade restrictions in colonial Africa. About a century after these unsuccessful colonial treaties, the WHO initiated the negotiation of a global strategy to control alcohol internationally. This strategy will be presented to the World Health Assembly and adopted in 2010. It will be of a lower legal status than the tobacco convention and will not be legally binding.

Compared to tobacco, alcohol is much less regulated, and compared to opium, coca, and cannabis, alcohol and tobacco are traded almost freely on the international level. The reasons why alcohol and tobacco are not as strictly controlled is that large industries are behind the production and distribution of these drugs and their use is socially integrated in most modern countries. Companies such as Philip Morris International or SABMiller are not only powerful political actors by themselves; they also bring large tax incomes to governments. Hence, it is understandable that drugs produced by such big economic players are not as tightly regulated as opium and coca. In addition, in contrast to opium and coca that are traditionally produced in Asia and

South America, global alcohol and tobacco production is concentrated in rich Western states, which have more bargaining power at international negotiation tables.

Only in the field of the global tobacco trade is it possible to see more controls in the near future. Not only is demand for this drug slowly decreasing in richer countries but also recent international agreements have directly attacked powerful economic interests. It is possible that the flourishing tobacco trade will face the same fate as the trade in opium, coca, and cannabis products confronted at the beginning of the twentieth century. However, if the international tobacco-control system will also prioritize the supply side of the trade and ignore health issues, the danger exists that it will lead to another failed international initiative, which merely strengthens the illegal trade in drugs.

See also **Afghanistan; China; Colombia; Crop Control Policies; Foreign Policy and Drugs, United States; Harm Reduction; International Drug Supply Systems; Opium: International Overview; Terrorism and Drugs.**

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GERNOT KLANTSCHNIG

INTERNATIONAL DRUG SUPPLY SYSTEMS.

While drug use and drug abuse have been a part of human cultures for thousands of years, the international drug control system to prohibit the trade in drugs such as opium and cocaine only began in the early 1900s. The first instrument of international law to deal with psychoactive drugs was the Hague Opium Convention of 1912. It required each signatory to enact domestic legislation controlling opium and cocaine so they could be restricted to medical use, thus beginning a process that evolved into the multilateral drug control system of the early twenty-first century. From these origins, a still-continuing process broadened and deepened the scope of control over drugs, from opium and cocaine to cannabis, LSD, amphetamines, Ecstasy, methamphetamines, and many other psychotropic substances.

The century since the Hague Opium Convention saw a number of illicit drug epidemics sweep across the world. The World Drug Report (2006) argued that there was evidence that the multilateral system had reduced and contained the drug problem at a global level because world opium production stood at 30,000 metric tons in 1907/1908 (before the convening of the Shanghai Opium Convention), and opium production had fallen to 5,000 tons in 2005, even though the world population had expanded from 2 billion to 6 billion. The problem with this comparison is that opium had widespread medical use in 1907; it was the basis for countless soothing syrups and popular panaceas in Europe and North America: Unless the percentage consumed for nonmedical use at that time is known, the comparison between production levels in 1907 with those in 2005 is pointless. As well, a fair inventory of the market for illicit substances in 2005 would need to include 45,000 tons of cannabis, 910 tons of cocaine, and 450 tons of amphetamine-like stimulants, as well as the 5,000 tons of opium. The nonmedical use of opium may have fallen over the century, but the use of cannabis and other drugs has increased enormously (UN Office on Drugs and Crime, 2006).

After the arms trade (with which it shares an unusual symbiosis), the illicit drug trade is the largest trade in the world, worth an estimated 1 to 2 trillion U.S. dollars. Ninety percent of this trade is based on three plants, the opium poppy (the source of heroin), the coca bush (the source of cocaine), and the cannabis plant. Cannabis is the largest of the illicit crops, and because of

hydroponics techniques, cannabis can now be grown almost anywhere. The cultivation of the coca shrub remains limited to western and northern areas of South America, whereas Afghanistan, southeast Asia, Mexico, and Colombia account for most of the world's illicit opium production. Although the U.S. drug market remains the largest global market and the United States is the destination for much of the global drug trade, Europe has emerged as a significant rival. The drug routes that begin in Afghanistan, southeast Asia, and Colombia snake their way across the globe to these two great markets where most of the tens of thousands of tons of cannabis and the hundreds of tons of heroin, cocaine, and amphetamine-like substances are consumed.

Heroin production declined in southeast Asia between 1995 and 2008, and one of the significant developments in the global illicit drug trade has been a move away from heroin production to methamphetamine production by southeast Asian criminal organizations to fuel the growing global methamphetamine market. Other major developments that shaped the global drug trade at the start of the twenty-first century were the rise of Afghanistan to a dominant position in the global heroin trade and the preponderance of hydroponics cannabis in the cannabis market.

OPIUM

The opium poppy (*Papaver somniferum*) is the source of heroin. It is grown in three principal geographic regions: southeast Asia, southwest Asia, and Latin America. After 1971, when modern international drug control efforts began, a number of major shifts occurred in the opium-producing capabilities of various countries. For example, in the early 1970s, after the so-called French Connection was broken (Turkish opium was processed into heroin in France), Mexico and southeast Asia replaced Turkey as the major source of U.S. heroin; Pakistan then supplanted Mexico after 1979, when the Soviet Union occupied Afghanistan, and the resistance movements there increased opium cultivation to generate income and finance the war.

In 1991, the southeast Asian Golden Triangle countries of Myanmar (Burma until 1989), Laos, and Thailand cultivated approximately 81 percent of the world's total opium, which would yield 250 metric tons of heroin. The Golden Crescent countries of Afghanistan, Iran, and Pakistan cultivated approximately 11 percent, and the Latin American countries of Mexico, Guatemala, and Colombia produced approximately 8 percent.

Figure 1, Global opium production (1990–2005) from the 2006 World Drug Report, shows

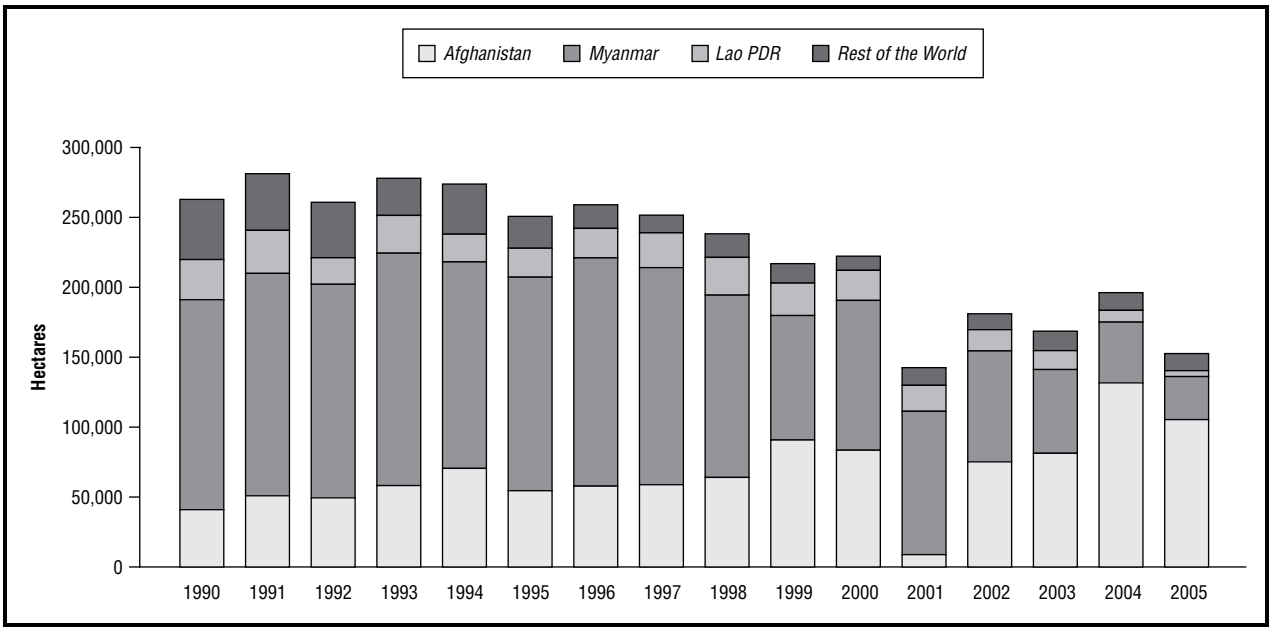

Figure 1. Global opium production (1990–2005). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

the gradual decline in southeast Asian heroin production between 1990 and 2005. This decline was due to environmental factors (a drought in Myanmar between 1997 and 1999) and also a preference for methamphetamine in the southeast Asian market. A spectacular decline in opium production occurred in Afghanistan between 1999 and 2001 from an estimated 89,172 hectares in 2000 to an estimated 7,606 hectares in 2001, a reduction of 91 percent. Afghanistan produced an estimated 79 percent of the world's illicit opium in 1999, but this dropped to 70 percent in 2000, following a decree issued by the Taliban authorities in September 1999, requiring all opium-growers to reduce output by one-third. A second decree, issued in July 2000, required farmers to completely stop opium cultivation. As a consequence, 2001 saw the lowest level of global opium production in the period. Perhaps not coincidentally, Australia experienced a spectacular heroin shortage in 2001. While opium and morphine seizures fell in Europe and Asia in 2001, the year of the opium poppy cultivation ban in Afghanistan, heroin seizures fell in 2002 (mainly reflecting a delay of about a year in the production of opium in Afghanistan and the arrival of heroin in western European markets). Opiate seizures grew strongly again in subsequent years.

Between 2002 and 2004, the proportion of opiate seizures along the Afghanistan-Europe trafficking route increased from 78 percent to 85 percent, reflecting rising levels of opium production in Afghanistan and rising levels of opiate trafficking from Afghanistan. The volume of opiate seizures along the other two main routes showed a downward trend (from 7% to 4% in the Americas and from 15% to 11% for the southeast Asia/Oceania route). Global opiate seizures in 2004 were 21 percent higher than in 2000. Over the 1994–2004 period opiate seizures grew, on average, by 8 percent per year. Europe's opiate seizure rose by 49 percent in 2004 and reached almost 29 metric tons (in heroin equivalents), the highest such figure ever recorded. While most of the opiates for the Commonwealth of Independent States (CIS) countries and some of the opiates for the Nordic countries were trafficked via central Asia, most of the opiates for western Europe were trafficked from Afghanistan to Turkey and then along various branches of the Balkan route. More than 90 percent of opiates in Europe originated in post-Taliban Afghanistan (after 2001).

While environmental and political factors had a detrimental effect on heroin production in southeast Asia, other changes in the Asian drug trade in the 1990s also contributed to the decrease in heroin production in the region. In China and Thailand, which are the major markets for producers in the Golden Triangle, heroin was displaced as drug of choice in the 1990s by *yaa-baa*, an amphetamine-type stimulant.

Yaa-baa was originally known in Thailand as *yaa-ma* (literally, horse medicine), but in 1996 Thai health minister Sanoh Thienthong substituted the name *yaa-baa* (madness drug) in order to disenchant the public with a product whose consumption levels had already reached alarming proportions. Not surprisingly, as *yaa-baa* the drug became even more popular. The thriving trade in *yaa-baa* stimulated methamphetamine production in Burma and Thailand and attracted players from heroin production. According to a 2004 study by Chouvy and Meissonnier, methamphetamine production was easier, more flexible, and cheaper than heroin production, and it did not need vast areas devoted to its production. Thus, methamphetamine manufacture was more attractive to many big players in the heroin market, and Chouvy and Meissonnier suggest that the very public retirement of Khun Sa and his United Wa State Army from the heroin industry in 1996 masked a move into methamphetamine production (Chouvy & Meissonnier, 2004).

CANNABIS

An estimated 4 percent of the world's adult population consumes cannabis each year, more than all the other illicit drugs combined. In some countries, more than half of the young people polled had tried it. However, when it comes to the mechanics of the market, the world's biggest illicit drug is the least understood. The advent of indoor cannabis cultivation techniques (hydroponics) in the last decades of the twentieth century revolutionized the cannabis market to the extent that cannabis can be grown virtually anywhere, and there are no countries where it can be definitively said that cannabis is not cultivated. Moreover, because cannabis is both easy to grow and highly productive, yielding a large quantity of ready-to-use drug per plant, many users can, and do, produce their own supply. Unlike other drug crops, illicit crop monitoring techniques, such as satellite surveillance, are of little use in assessing

cannabis cultivation, which is taking place in private homes and small plots in communities spread across the globe. As a consequence, this critical sector of the cannabis trade is almost invisible. Few governments can confidently give an estimate of the scale of cultivation in their own countries, and even in the United States, a country with both resources and a strong infrastructure for cannabis control, official estimates of the extent of domestic cultivation vary considerably.

However, the evidence of cannabis seizures show that, in terms of both volume and geographic spread, cannabis remains the most widely trafficked illicit drug in the world, accounting for the majority of all illicit drug seizures. Globally, herbal cannabis (marijuana) seizures surpassed the 6,000 metric ton mark in 2004, and an additional 1,470 metric tons of cannabis resin (hashish) were seized. Cannabis seizures were reported from 176 countries and territories (90% of the UN list), and the UN estimated global cannabis production was 45,000 metric tons. Cannabis was almost ubiquitous, trafficked in nearly every country in the world, and the upward trend in cannabis seizures, which began in the early 1990s, continued in 2004. Most herbal cannabis seizures were reported from Mexico, followed by the United States, South Africa, Nigeria, and Morocco, whereas most seizures of cannabis resin were made by Spain, followed by Pakistan, France, Morocco, and Iran. While cannabis resin (hashish) retained its traditional popularity in Eurasia and north Africa, herbal cannabis dominated in the markets of the Western hemisphere and grew in popularity in Europe and Africa.

Most of the global total of cannabis herb was seized in North America, notably Mexico and the United States. With seizures of 2,164 metric tons in 2004, Mexico accounted for 35 percent of global seizures, followed by the United States, where 1,118 metric tons of cannabis herb were seized in 2004. North America dominates the world cannabis market, and, as a consequence of hydroponics technology, the cannabis markets in North America have become largely self-sufficient.

According to the United States Office of National Drug Control Policy estimates (which are about 30% lower than UN estimates), 10,100 metric tons of cannabis herb were produced in Mexico in 2005. This estimate made Mexico the largest cannabis herb producer in the world. In the United States, about 4,455 metric tons of cannabis herb were produced in fiscal year 2004–2005, while an estimated 800 metric tons of cannabis herb were produced in Canada.

In the late 1980s and early 1990s, herbal cannabis was chiefly grown in tropical and subtropical climates. For example, in 1990 South America accounted for 46 percent of global herbal cannabis seizures, but this share fell to 7 percent in 2004. However, hydroponics technology enabled Canada, and its western province British Columbia in particular, to become a major producer and supplier to the U.S. market. The hydroponics revolution, which transformed cannabis production so that cannabis can be grown indoors almost anywhere, radically transformed the U.S. cannabis trade, allowing cannabis to be grown in countries closer to the U.S. market and disadvantaging traditional suppliers in South America and the Caribbean.

Despite this change, Colombia continued to be the major cannabis producer in South America with an estimated production of 2,000 metric tons, though its role as a supplier of the U.S. market declined as a consequence of the hydroponics revolution. Colombia's decline was accelerated by the extensive crop eradication programs conducted by the United States and the government of Colombia beginning in the 1980s. Paraguay emerged as the second-largest producer in South America, with much Paraguayan cannabis destined for the Brazilian market.

African cannabis production increased significantly between 1990 and 2004: African seizures were 16 percent of global herbal cannabis seizures in 1990; 20 percent in 2002; and 31 percent in 2004. The major producing countries of cannabis herb in Africa, according to UN estimates, were Morocco (3,700 metric tons), South Africa (2,200 metric tons), and Nigeria (2,000 metric tons). Morocco was also the world's largest producer of cannabis resin, producing an estimated 40 percent of global production. The area under cannabis cultivation in Morocco decreased significantly by 40 percent from 120,500 hectares to 72,500 hectares in 2004, largely due to a severe drought. Eradication campaigns in the provinces of Larache, Tanouate, and Chefchaouen, targeting over 15,000 hectares of cannabis in total, further decreased Morocco's total production figure for cannabis.

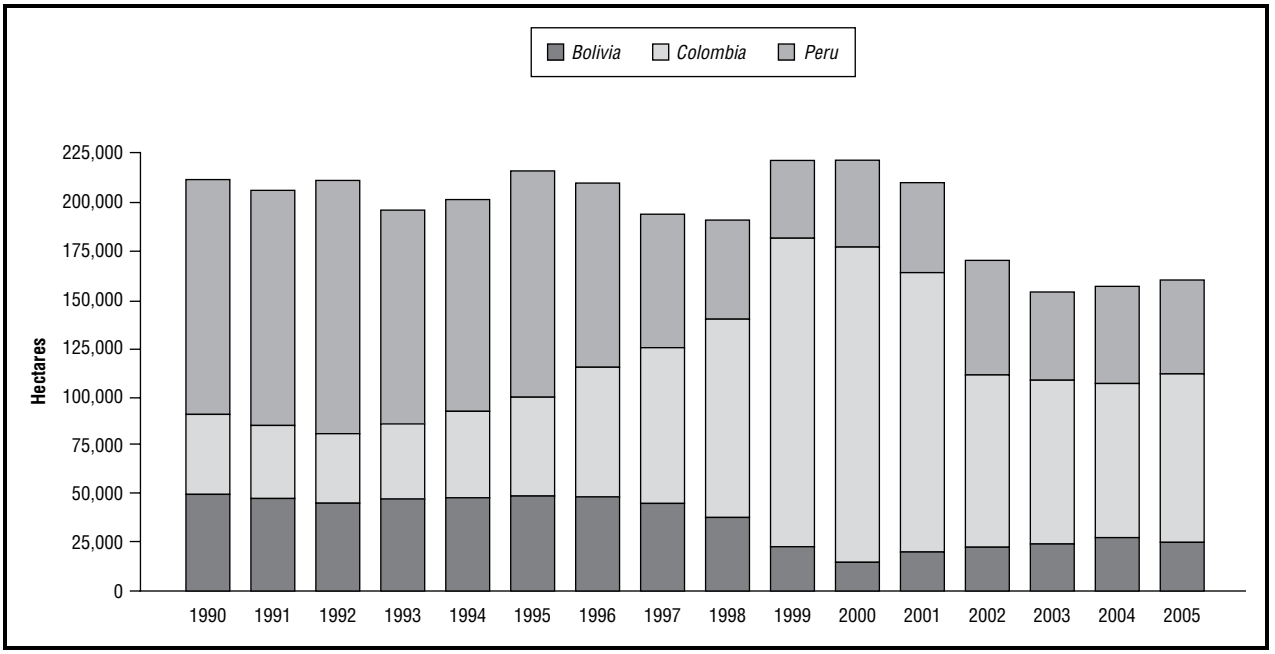

Figure 2. Global Coca Bush Cultivation (in ha), 1990–2005. (Source: Columbian government with support from the United Nations Office of Drugs and Crime.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Cannabis use is traditional in Asia, and many Asian countries produce considerable quantities of cannabis: Lebanon, Turkey, Kazakhstan, Kyrgyzstan, Afghanistan, Pakistan, India, Sri Lanka, Myanmar, Cambodia, Thailand, and the Philippines are major Asian markets which produce annually between 300 and 1,500 metric tons of cannabis.

Cannabis Resin (Hashish). Three subregions accounted for 99 percent of global cannabis resin seizures: west and central Europe (74%), near and middle east/southwest Asia (18%), and north Africa (7%). The largest seizures worldwide were reported by Spain (794 metric tons or 54% of the total), followed by Pakistan (135 metric tons or 9%), Morocco (86 metric tons or 6%), and Iran (86 tons or 6%). In Afghanistan, cannabis resin seizures declined by almost half, from 81 tons in 2003 to 41 tons in 2004. In Algeria, seizures of some 12 tons of cannabis resin were reported for 2004, more than double the quantity seized in 2002.

The main destination of cannabis resin is west and central Europe. About 80 percent of the cannabis resin destined for the European market was estimated to originate in Morocco. As of 2008, much of the cannabis resin transited Spain and the Netherlands before being shipped to other countries. The remainder of the resin supply originated in Afghanistan/Pakistan, central Asia (which mostly supplies the Russian Federation, other CIS states, and some of the Baltic countries), or from within Europe (mainly Albania, supplying the markets of various Balkan countries and Greece).

The second-largest destination of cannabis resin is the near and middle east/southwest Asia region. This region is mainly supplied from cannabis resin produced in Afghanistan and Pakistan and, to a lesser degree, from cannabis resin originating in Lebanon. Some of the cannabis resin from Afghanistan/Pakistan was as of 2008 also being shipped to Canada and to countries in eastern Africa. North Africa makes up the third-largest market and is predominantly supplied by cannabis resin produced in Morocco. The importance of other markets is limited. Nepal is a source country for cannabis resin exports to India and to some other countries, and Jamaica is a source country for cannabis resin exports to some other countries in the Americas.

COCA/COCAINE

All of the cocaine consumed in the world is grown and processed in the Andean countries of Peru, Bolivia, and Colombia. In 2005, an estimated 160,000

hectares of coca was under cultivation in these three countries. Most coca was cultivated in Colombia (54%), followed by Peru (30%) and Bolivia (16%). Much of this crop was smuggled across the Caribbean Sea or the Mexican border into the United States, though increasing amounts were transshipped to Europe via Africa.

Colombia. Vast tracts of uncontrollable land, a seemingly endless civil war, powerful criminal organizations, and a long tradition of smuggling, all helped Colombia become the center of the cocaine trade. Although other Andean countries have sometimes produced more coca, Colombia's proximity to the U.S. marketplace has meant that Colombia's drug cartels are the world's leading producers of both cocaine HCL (which is sniffed or snorted) and *crack* (which is smoked).

As of 2008, Colombian cocaine-trafficking organizations were sophisticated and well-organized industries, which derived their strength from control of cocaine laboratories and the smuggling routes to Europe and North America. They sometimes financed the cultivation of coca plants in Bolivia, Peru, and Colombia, often overseeing the processing of the leaves into coca paste and sometimes base, which may then be shipped to laboratories in Colombia where the traffickers refine the coca paste, first into coca base and then into cocaine by the ton.

The Office of National Drug Control Policy estimated the 2006 coca cultivation in Colombia was stable at between 125,800 and 179,500 hectares. After losing one-third of the estimated coca cultivation to herbicidal spraying between 2001 and 2004, traffickers and growers implemented the widespread use of techniques such as radical pruning, replanting from seedlings, and a move to smaller plots. Such countermeasures made it impossible for forecasters to know with certainty whether a field was a mature, productive field or a field that had been sprayed with glyphosate and then pruned or replanted. Moreover, farmers have expanded cultivation into areas off-limits to the spray program, such as national parks and the area along the border with Ecuador, where Colombia suspended spraying in 2006 due to protests from the Ecuadorian government.

Colombia's antidrug efforts also affected the Fuerzas Armadas Revolucionarias de Colombia (FARC).

The governments of Colombia, the United States, Canada, and the European Union describe the FARC as a terrorist organization. Those of Cuba and Venezuela call it a rebel insurgency. As of 2008 the organization depended on drug trafficking, kidnapping, and theft to sustain itself. FARC rebels trained and equipped to shoot down unarmed spray planes have required the deployment of armed security helicopters and search-and-rescue aircraft in the vicinity of spray operations. FARC leaders protect growers who cooperate with them and force others to grow; strengthening their control over the population through economic dependency. The U.S. Government, working with Colombia, shifted the focus of its aerial eradication to target the areas of most intensive coca cultivation.

Peru. Peru is the world's second-largest cocaine producer. The Office of National Drug Control Policy (ONDCP) estimated that Peru's coca cultivation in 2006 ranged from 31,000 and 42,800 hectares and estimated potential cocaine production was 245 metric tons. Considerable political controversy has erupted in both Peru and Bolivia over U.S. backed counternarcotics strategies, particularly coca eradication. Coca leaf (but not cocaine) is a traditional medicine and is legal in Peru and Bolivia. The growers of coca (who are called *cocaleros*) oppose coca eradication and the election of several new cocalero members to Peru's Congress raised the profile of the debate surrounding coca cultivation and amplified the voice of organized, politically active cocalero groups working to stop eradication. Although the attempts by the Peruvian National Police to eradicate coca cultivation in the valleys were disrupted by growers who resisted programmed eradication, the government of Peru exceeded its 10,000-hectare eradication goal: It eradicated 12,688 hectares of coca in 2006 and interdicted over 19 metric tons of cocaine.

Bolivia. Bolivia is the world's third-largest cocaine producer and is a country of concern for U.S. policy makers because coca farmers (cocaleros) led by President Evo Morales have called for an end to forced eradication and other antinarcotic measures. Morales rose to national attention by leading the political opposition to eradication, and his opposition was a central reason for his election to the Bolivian Congress. His association with anti-eradication forces

caused his expulsion from Congress in 2002 and led to his presidential campaign. Upon entering office in January 2006, President Evo Morales advocated a counternarcotics policy of *zero cocaine*, *revalidation* of the coca leaf, and repeatedly called for legalization and industrialization of the coca leaf in international forums. While Bolivia met its self-established coca eradication goal of 5,000 hectares in 2005, the 2006 effort represented the lowest level of eradication in more than ten years. Bolivia failed to conduct a study to determine licit demand for coca and rejected the European Union offer to provide full funding support for such a study. President Morales announced his intention to increase the amount of hectarage allowed for legal coca cultivation from 12,000 to 20,000. The government of Bolivia announced it would permit 8,000 hectares of coca in the Chapare region, an increase of about 17 percent, consistent with President Morales's move to permit 20,000 hectares of cultivation.

Although there is much disagreement between Morales's administration and the United States regarding antidrug laws and cooperation between the countries, officials from both countries have expressed a desire to work against drug trafficking with Morales calling for zero cocaine and zero drug trafficking. The government of Bolivia interdicted more than 14 metric tons of cocaine base and HCl in 2006, up from 11.5 metric tons in 2005. The Office of National Drug Control Policy (ONDCP) estimated Bolivia's coca cultivation at between 21,000 and 32,500 hectares. Cocaine potential production remained unchanged at 115 metric tons from 2005 to 2006.

AMPHETAMINE-TYPE STIMULANTS (ATS)

The group of amphetamine-type stimulants (ATS) encompasses amphetamines (amphetamine, methamphetamine), Ecstasy (MDMA and related substances), and other synthetic stimulants (e.g., methcathinone, phentermine, fenetylline). The *World Drug Report 2006* estimated total ATS production at about 480 tons: 290 tons of methamphetamine, 63 tons of amphetamine, and about 126 metric tons of Ecstasy (MDMA). Most of the amphetamine production took place in Europe; most of the methamphetamine production occurred in North America and east and southeast Asia, and most Ecstasy was produced in Europe and in North America.

The number of globally dismantled ATS laboratories, as reported to UNODC, increased from 547 in 1990 to 7,028 in 2000 and to a record high of 18,532 in 2004. The increase was a reflection of the growth in ATS production globally since the 1990s: Methamphetamines and Ecstasy were the most recent drug epidemics. The overwhelming majority of dismantled ATS laboratories were producing methamphetamine, but 86 Ecstasy laboratories were seized, up from 64 in 2000 and 15 in 1999.

The overwhelming majority of the methamphetamine laboratories (97%) were dismantled in North America, mainly the United States, and, to a lesser extent, Mexico. Methamphetamine laboratories were also dismantled in Oceania, in east and southeast Asia, in Europe (mainly Czech Republic, followed by Slovak Republic and Republic of Moldova) and in South Africa (which appeared as of 2008 to be emerging as an important local production center). In Asia, most methamphetamine laboratories seized over the 2002–2004 period were reported from China, Philippines, Taiwan Province of China, Myanmar, Hong Kong SAR of China, and Malaysia. Many of the chemical precursors for ATS production originate in east and southeast Asia, and the switch away from heroin to ATS production by southeast Asian gangs in the 1990s was one of the motors of the methamphetamine epidemic.

Europe's position as the world's main Ecstasy production center appeared to be on the decline, with production shifting to North America (mainly United States and Canada): 48 percent of all Ecstasy laboratories were seized in North America (United States and Canada), and only 23 percent in Europe (mainly Netherlands, followed by Belgium and Estonia), down from 75 percent in 2000. Over the 2002–2004 period, Ecstasy laboratories were dismantled in southeast Asia (Indonesia, China, Hong Kong SAR of China, Malaysia), in Oceania (Australia and New Zealand), in Africa (South Africa and Egypt), and in some South American countries (Argentina in 2003 and Colombia in 2001).

Methamphetamine. The main countries of origin for methamphetamine production in Asia continue to be China, Myanmar, and Philippines. Most of the methamphetamine production in China was located in southeastern China, in Guangdong

Province (which surrounds Hong Kong SAR of China), and, to a lesser extent, in neighboring Fujian province, located off the coast of Taiwan Province of China. China, together with India, is also one of the main source countries of ephedrine and pseudoephedrine, the main precursor chemicals used to manufacture methamphetamine. Significant quantities of methamphetamine were manufactured in Taiwan and the Philippines. Myanmar also continued to play an important role as a production site for methamphetamine. Illicit markets in Thailand were supplied by methamphetamine produced in Myanmar, and important parts of the Chinese market (20%) were also supplied by methamphetamine produced in Myanmar. ATS production in Myanmar was mainly encountered in the Shan state (notably in the Wa region) bordering China, though production was also taking place in areas controlled by the ethnic Chinese Kokang, the Shan State Army-South, and the Kachin Defense Army (KDA). Production was sometimes colocated with heroin refineries. According to the government of Thailand, methamphetamine production largely ceased to exist in Thailand following the crackdown on the market in 2003. Most southeast Asian methamphetamine was trafficked toward Oceania, notably Australia and New Zealand, and North America. The Philippines and China have been identified as other source countries for southeast Asian methamphetamine found on North American markets. Southeast Asian methamphetamine, from Myanmar and the Philippines, crossed Thailand before it was trafficked to European destinations, mainly the United Kingdom, Netherlands, France, and Switzerland.

Large-scale methamphetamine production and consumption had as of 2008 not occurred in Europe where Ecstasy dominated the ATS market. European methamphetamine production continued to be largely limited to the Czech Republic and, to a lesser extent, the neighboring Slovak Republic, some of the Baltic states, and Moldova. Limited imports of methamphetamine from southeast Asia (Thailand and Philippines) were reported in the late 1990s and early twenty-first century.

The main countries of methamphetamine production in the Americas are the United States, followed by Mexico and Canada. U.S. authorities dismantled the largest numbers of methamphetamine laboratories worldwide in 2004 (97%). Methamphetamine production in the United States was once concentrated in California and several neighboring states, but it spread to most states. Most of the *super-labs*, that is, laboratories capable of manufacturing more than 5 kg of methamphetamine in 24 hours, continue to be located in California. In Mexico, which reported the dismantling of 18 laboratories to UNODC in 2004, most methamphetamine production took place in the northern part.

Overall production of ATS was limited in South America (where coca and cocaine dominated the stimulant market) and in central and northern Africa, where *khat* had a similar dominance. (Khat [*Catha edulis*], a flowering plant native to east Africa and the Arabian Peninsula, contains the alkaloid cathinine, an amphetamine-like stimulant.) The main exception was South Africa where ATS production, notably production of methamphetamine and methcathinone, increased substantially.

Ecstasy. Over the 2002–2004 period a total of 33 Ecstasy-producing countries were identified by UNODC member states. The Netherlands and Belgium were the main countries of origin for Ecstasy imports over the 2002–2004 period. But their importance as the main source countries for Ecstasy was declining. The decline of Ecstasy production in eastern Europe, however, appeared to have been offset by increasing levels of Ecstasy produced in other countries, including other European countries, countries in North America (United States and Canada), in the Oceania region, and in east and southeast Asia, indicating that a shift toward Ecstasy production outside the so-called traditional production centers in Europe was gaining momentum. Though production may have well declined in the largest Ecstasy-producing center (Netherlands) and consumption fell in the world's single largest Ecstasy market (United States), the overall trend in global Ecstasy production was upward.

The increasing number of countries where clandestine ATS laboratories were dismantled indicated that ATS production was spreading in geographical terms. Nonetheless, there remained clear concentrations of ATS production in North America, east and southeast Asia, and in Europe.

See also **Afghanistan; Amphetamine Epidemics, International; Bolivia; China; Coca/Cocaine, International; Colombia; Drug Interdiction; European Union; Golden Triangle as Drug Source; Mexico; Middle East; Money Laundering; Operation Intercept; Opium: International Overview; Peru; Terrorism and Drugs; U.S. Government Agencies; U.S. Government; World Health Organization Expert Committee on Drug Dependence.**

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JOHN JIGGENS

INTERNET: IMPACT ON DRUG AND ALCOHOL USE.

The impact of the Internet on drug and alcohol use has been both positive and negative. On the one hand, it has been the vehicle for important, accurate information on the effects and impact of drugs, including alcohol; has provided the conduit for community organization around drug and alcohol prevention issues; and has served as a virtual training platform for professionals and others involved in drug abuse prevention, rehabilitation, and treatment. On the other hand, it has been the vehicle for directly or indirectly persuading others to experiment with new substances or modifications; has provided explicit information regarding how to grow marijuana and make synthetic drugs, crack cocaine, and various combinations of synthetic and naturally derived drugs; and has been the commercial vehicle for the selling of illegal drugs.

INTERNET SOURCES FOR POSITIVE INFORMATION ON DRUGS

For a concerned parent, teacher, community leader, health professional, drug user, or potential drug user, there is a wealth of factual, scientifically based information available regarding the general nature and extent of drug and alcohol use; information on specific drugs, including alcohol; and guidance for families, and the vulnerable populations of teens, women, seniors, and others. Among other organizations, the federal government's Substance Abuse and Mental Health Services Administration (SAMHSA), a division of the Department of Health and Human Services, provides the broadest range of current research and other information. This administration maintains a number of websites. For the individual interested in or concerned about the effects of a particular drug, current and timely information available on the Internet indicates the short-term, carryover, and long-term effects of the drug. For families that are concerned about their children's vulnerability to drugs, there are guides for parents and children, as well as community organization information for those with a shared interest in drug and alcohol prevention. The information is free. Either online or in printed copy through the National Clearinghouse for Drug and Alcohol Information at the website maintained by SAMHSA or from a steadily growing number of resource sites sponsored by state and local governments and by volunteer and advocacy groups that focus on one or more aspects of drug and alcohol prevention.

INTERNET USES FOR COMMUNITY ORGANIZATIONS

Communities and other groups use the Internet to facilitate their drug and alcohol prevention efforts. There are literally hundreds of websites that provide information regarding drug and alcohol prevention. Many target teens in general, but there are also sites for specific groups, such as Hispanic and Asian families, pregnant women, youth in high-risk neighborhoods, rural youth, and Native Americans. Families or individuals who need help can find a wealth of information regarding treatment and other helping programs that are available in any given location.

Physicians and other health practitioners also use the internet to obtain information. Online journals, legacy medical and professional journals from which

articles can be downloaded, and recent studies published by the National Institute on Drug Abuse (NIDA), a part of the National Institutes of Health (NIH), and SAMHSA, are all available online.

The Internet has provided the basis for comprehensive workplace drug and alcohol testing because of its ease of access and the application of proprietary security programs as a part of employer efforts. From government mandated drug and alcohol testing programs, such as those required by the Department of Transportation for safety-sensitive positions in the airline, railroad, mass transit, pipeline, trucking and busing, and maritime industries, the internet permits flexible scheduling for testing at any location, ease of transmission of test results from the drug testing laboratory to the employer, the ability to rapidly organize and transmit drug testing information to those physicians responsible for their review (medical review officers). As of 2008, over 8 million workplace drug tests were performed annually (Quest Diagnostics, 2008). Most of these are managed through an interactive Internet process that involves selection of people for random testing, where applicable; the scheduling of testing; laboratory results; and where not negative, a report from the medical review officer to the employer regarding the disposition of the test.

TWO APPROACHES TO PREVENTION

The internet plays a pivotal role in helping prevention groups mobilize. As of 2008, within the United States and internationally, there are two major approaches to drug abuse prevention. One approach favors a no-tolerance policy that promotes abstinence for the non-user through family, school, and other prevention efforts (e.g., information, education and drug and alcohol testing programs, and treatment and counseling for those who are using drugs). This approach encompasses empowering families and communities to reach out to their stakeholders through informal and formal education and intervention efforts but also includes legal and other tripwire efforts to identify the regular users through random drug testing programs in the schools, law enforcement referrals of drug offenders to treatment, and the use of drug courts and other approaches designed to identify and refer users to programs whose goals are abstinence recovery.

The second approach supports the concept of *harm reduction*, the major premise of which is that the prohibition of drug use is discriminatory, ineffective, and counter-productive. This approach asserts that rather than stigmatize a person for drug use, programs should be established that reduce the harm caused by the drug use and hence reduce the stigma attached to that drug use. People who believe in harm reduction often support some or all of the following: needle exchange; safe shooting houses; other safer-use techniques; heroin maintenance; drug legalization; and the use of street marijuana in certain medical situations. They believe these strategies mitigate public health costs of drug use. Critics call this approach *harm promotion*, asserting that while harm reduction attempts to reduce the physical consequences of drug use it does not reduce the use of legal and illegal drugs.

While harm reduction groups receive significant funding from wealthy libertarians and others, the opposition groups are largely spontaneously formed organizations that have a local or regional interest or are established by volunteers who have lost family members because of drug use. Both sides use the internet aggressively to support or oppose legislation at the local, state, and national level that would support harm education efforts, especially legislation that supports the use of street marijuana for medical purposes, which the harm reduction supporters see as a form of compassionate care for the severely or terminally ill, while prohibitionists see it as a move that may lead to legalization of marijuana. Both sides use the internet to alert their supporters of proposed or pending legislation, mobilize email and other campaigns to inform legislators of their positions, and contact media, especially newspapers, to provide substantiation of their position. The factors stated above that make the internet ideal for commerce also apply here. Hundreds of emails a day can be generated on any issue and disseminated to thousands of people. The consequence is that robustly funded harm-reduction initiatives are often thwarted by aggressive grassroots messages aimed at legislators and other policy makers by the abstinence community.

INTERNET INFORMATION LEADING TO ILLEGAL ACTIVITIES

The availability of information cuts two ways. While the internet provides helpful information

for those wanting to prevent drug and alcohol use, it also provides information that tempts some people to use drugs or continue using them. As of 2008 websites promoting drug use were on the decline; however, individuals could still locate so-called friendly blogs, forums, and news group that provide anecdotal information about the effects of old or new street drugs. Recipes for making a range of drugs from gamma hydroxybutyric acid (GHB, a synthetic depressant) and lysergic acid diethylamide (LSD, a semisynthetic psychedelic) to methamphetamine were also available online. Websites for the purchase of marijuana seeds and accoutrements for a successful harvest abound.

The internet has been a viable method of selling illegal drugs. It is always accessible and affordable; anyone can tap on from anywhere in the world, and one can hide activities with ease. The Wide World Web also lowers transaction costs dramatically. Until 2003, it was exceptionally easy to purchase illicit pharmaceuticals on the internet. Dozens of sales sites existed, some of them legitimate (such as Internet Pharmacies), but many of them sham fronts for illegal sales. While many purported to require a physician's approval, most off-shore sites only required some general health information and a self-certification of need or a brief medical questionnaire filled out. By 2004, the federal government recognized the significance of Internet-selling and began an intensive program to reduce these U.S. rogue sites. As of 2008 there were still a few rogue sites in the United States. However, no websites had been found selling illegal drugs such as heroin, or illegal amphetamine derivatives.

RESEARCH OF THE INTERNET

One study concluded that Web-based data on psychoactive substances seem to influence a broad range of drug-use behaviors in adolescents (Quest Diagnostics, 2008). The study stated:

> participants . . . adopted new behaviors such as modifications in the use of preferred drugs, the cessation of psychoactive substance abuse, and the use of new drugs and drug combinations. The striking finding from [this] study, therefore, is that all respondents in [the] cohort modified their drug use after reviewing online drug information. This observation suggests that the Internet has a profound ability to affect decisions related to psychoactive substance use in a cohort of innovative drug users. Interestingly, [two-thirds of the] participants adopted behaviors intended to minimize the risks associated with drug use, a finding that suggests that attempts to reduce the harm associated with psychoactive substances are fostered by online information.

Another study documented the fact that teens use the internet to share drug stories. A study commissioned by the Caron Treatment Foundation on teenage messages about drug use written on the internet establishes that young people regularly chat about drinking alcohol, smoking pot, partying, and hooking up (Boyer et al., 2005). The major conclusions of the study are as follows:

1. Teens focus their discussion of alcohol and drug use on message boards, rather than on blogs or online groups—due in part to privacy concerns. Young adults, however, discuss drugs and alcohol use on their blogs. Older teens and college students post anecdotes, memories, and plans about recreational drinking in their online journals.
2. When teens do post about drugs or alcohol on their blogs, it is usually in the form of a quiz about past experiences. These quizzes usually ask participants to check off drug-use experiences they have had.
3. Many teen messages about drugs and alcohol overlap. Many teenagers discuss topics such as getting together with friends to drink and smoke marijuana, or they share their experiences of getting drunk and/or high.
4. Certain topical themes recur across each subject (alcohol, marijuana, other drugs). Whether discussing alcohol, marijuana, or other drug use, teens express concern for their friends/significant others, discuss their parents' opinions on drugs and alcohol, and warn each other about the dangers of substance abuse.
5. Teens ask more questions about other drugs than they do about alcohol or marijuana. While they were curious about experimenting with alcohol and marijuana, they seek information about other recreational drugs, such as Ecstasy, dextromethorphan (DXM), and shrooms (mushrooms). Teenagers ask other teens about the drugs' effects, sensations of being high, and dosage levels.

The 2005 Partnership for a Drug-Free America teen attitude survey of over 7,000 teens nationwide

indicated that almost one-third of the teens responding said that drugs were easy to purchase on the internet (Caron Treatment Centers, 2007).

In a 2002 *Evaluation of the National Youth Anti-Drug Media Campaign* approximately 10 percent of surveyed youth ages 12 to 18 visited anti-drug internet sites while approximately 5 percent of that same cohort visited pro-drug Internet sites. While both males and females visited the anti-drug sites at about the same rate, males were almost twice as likely to visit pro-drug sites. African American youth were most likely to visit antidrug sites, though whites and Hispanics also visited them to a significant degree. However, whites and Hispanics were almost twice as likely to visit pro-drug sites as African Americans (Partnership for a Drug-Free America, 2006). A similar study suggested that women are more likely to procure information from face-to-face encounters, whereas men prefer using online information outlets (Westat & Annenberg School for Communication).

SMOKING CESSATION RESEARCH VIA THE INTERNET: A FEASIBILITY STUDY

The Smoking Cessation Research via the Internet Study demonstrated the feasibility of conducting a brief, self-help smoking cessation intervention over the internet, using a one-group, pre-post design. The website was constructed to recruit participants, obtain informed consent, collect assessment data, provide a brief educational intervention, and obtain 1-month follow-up data, all without human contact. Of the 538 participants who signed the consent form, 230 returned to complete the one-month follow up assessment. Among these individuals, 92 made a serious attempt to quit smoking and 19 reported seven-day abstinence. Intention to quit smoking increased by 67 percent from baseline while 75 percent reported that they found the site helpful for quitting goals. The findings suggest that the Web is a practical environment for delivering and evaluating smoking cessation interventions. More research is needed on internet interventions, particularly on procedures to retain users for treatment and follow-up assessment. Internet interventions have the ability to treat large segments of the smoking population in a cost-effective manner (Stoddard et al., 2005).

See also **Media; Movies; Music.**

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RICHARD BUCHER

INTIMATE PARTNER VIOLENCE AND ALCOHOL/SUBSTANCE USE.

The potential links between psychoactive substances and violent behavior, and specifically violence against a spouse or intimate partner, have long been recognized. Historically, much of the focus has been on alcoholic beverages, rather than other psychoactive substances. For example, Netzahualcoyotl, king of a small city-state called Texcoco in Pre-Conquest Mexico c.1472 CE, stated "It [alcohol] is like a tornado that destroys everything in its path. It is like a hellish tempest that brings with it all evils. Drunkenness . . . causes violence among kinfolks" (Soustelle, 1955; cited in Paredes, 1975). In the United States, early temperance tracts emphasized the deleterious impact of alcohol on the family. The Fifth Report of the American Temperance Society states that "in the State of New York alone, in the course of a few weeks, not less than four men, under the influence of ardent spirits, murdered their wives." The 1843 *Temperance Tales, or, Six Nights with the Washingtonians* by Timothy Shay Arthur describes alcohol as a cause of moral decay and presents the final step in this decline with an illustration with the caption "the Husband, in a fit of furious drunkenness, kills his wife." Historical references linking other psychoactive substances to violence generally, or intimate partner violence more specifically, are few. However, in the twentieth century and continuing into the twenty-first century, substances, including cocaine and amphetamines, hallucinogens, and occasionally marijuana and opiates, have been anecdotally linked to violence, although few have been as consistently linked to violence as alcohol.

DEFINITION, PREVALENCE, AND EPIDEMIOLOGY OF INTIMATE PARTNER VIOLENCE

The broadest definition of violence is provided by the World Health Organization (1996) as "the intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, that either results or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment, or deprivation." A similar term, aggression, reflects "any behavior directed toward another individual that is carried out with the . . . [immediate] intent to cause harm" (Anderson & Bushman 2002, p. 28) with violence being viewed as "aggression that has extreme harm at its goal" (p. 29). While these definitions can include verbal or psychological aggression as well as sexual aggression, intimate partner violence most typically refers to behaviors that have the potential to physically harm or injure one's partner.

Intimate partner violence (IPV) encompasses behaviors ranging in severity from those that result in no discernible injury to those that result in the need for medical attention or result in death. According to the Department of Justice, there are 1,500 instances of homicide and manslaughter between intimate partners each year with more than 1,200 of these involving women as victims (BJS, 1998). Annually, approximately 200,000 women and 39,000 men are seen at an emergency room for injuries resulting from partner violence (National Electronic Injury Surveillance). The National Crime Victimization Survey estimated that nearly 600,000 women and more than 150,000 men were victims of intimate violence in 2001. The 1985 National Family Violence Resurvey of a representative sample of couples—which include less severe instances of aggression, such as single occurrences of pushing or slapping one's partner—reported an annual rate of husband to wife violence of 11.6 percent with rates of wife to husband violence at 12.4 percent (Straus & Gelles, 1990), which suggests that approximately 6.2 million women had been assaulted by their husbands; about 6.6 million men by their wives.

Many couples report that both the man and woman have engaged in partner violence. While there is considerable controversy regarding the meaning of these findings, it is generally recognized that some couples are characterized by mutual husband and wife

partner violence, whereas in other couples, partner violence is primarily displayed by either the husband or the wife, with the other person refraining from violence, engaging in substantially less violence, or using violent behaviors only in defense.

Several important risk factors for partner violence exist other than alcohol and drugs. For example, partner violence rates are highest among individuals under thirty years of age (McLaughlin, Leonard, & Senchak, 1992) and decline throughout the lifespan of the individuals (Suiter, Pillemer, & Straus, 1990). In addition, most aggression in marriage has an early onset, often prior to or in the first year of marriage. Couples who do not display aggression during this time are not likely to display aggression subsequently. In contrast, among couples who behave aggressively early in marriage, a large percentage display aggression at some time later in their marriage. Relatively few initially aggressive couples are consistently aggressive throughout the early years of marriage, though the degree of consistency is greater among individuals who have displayed severe levels of aggression. Finally, although there may be some decreases in marital aggression over the early years of marriage, the extent of these decrements is modest (Leonard, 2001). In addition to these factors, many sociodemographic and individual difference factors have been explored as potential risk factors for intimate partner violence (Schumacher, Feldbau-Kohn, Slep, & Heyman, 2001). Factors that have been consistently linked to partner violence by men include socioeconomic status, experiencing or witnessing family violence as a child, hostility, psychological (verbal) aggression, aggression-supportive attitudes, and a variety of different types of psychopathology. In addition, stress, jealousy, and relationship power have also been linked to partner violence. Many of these factors are associated both with partner violence and with alcohol and substance use.

CRITICAL ISSUES IN ALCOHOL/SUBSTANCE USE

Alcohol and other substances may affect intimate partner violence either through their acute psychological and psychopharmacological impact, or they may have an effect only in the context of the chronic pattern of use (e.g., average daily use, typical use). Acute effects refer to the impacts of the substances only when they are present and pharmacologically active in the user. Although one may consider the short-term psychophysiological state that occurs after the substance is no longer present (i.e., hangover, withdrawal) an acute effect, little research has focused on how this state affects partner violence or violence more generally. Chronic effects occur as a result of the pattern of use. For example, excessive use may lead to increased marital conflict and, through this conflict, increase the probability of intimate partner violence. These chronic effects may include the long-term chronic impact of substances. Among those who chronically use alcohol or other substances excessively, there may be considerable amounts of time when they are free from the acute effects of the substances.

Another issue is the considerable overlap between the use of alcohol and the use of other substances, both at acute and chronic levels. This overlap is important, particularly in clinical or especially severe samples. For example, an individual with very heavy alcohol use may also use marijuana and cocaine. Similarly, some individuals mix substances or use one substance to ease the effects or withdrawal of another substance. Disentangling the effects of these different substances can be challenging. Small samples of individuals who use only a single substance can suggest the acute or chronic effects of that single substance, but these inferences may not be generalizable to samples that use multiple substances.

EXPLANATIONS OF THE RELATIONSHIPS BETWEEN ALCOHOL OR SUBSTANCE USE AND PARTNER VIOLENCE

There are four broad explanations of the impact of substances on intimate partner violence, one which argues that the relationship is spurious, one that focuses on chronic aspects of alcohol/substance use, and two which focus on the acute impact of alcohol/substance use.

Spurious Association. One explanation argues that the association is spurious, with both alcohol/substance use and partner violence being associated with a third variable that is, in fact, the most critical factor. In this regard, the critical variable is often viewed as hostile and/or antisocial personality traits. Evidence links hostile, antisocial traits to partner violence, and these factors contribute to

the association between alcohol/substance use and partner violence. However, some studies of excessive alcohol use have taken these factors into account and have found a relationship between excessive drinking and partner violence occurrence or severity. As of 2008 findings from studies on substance use that have controlled for hostile, antisocial traits have not been entirely consistent.

Chronic Use Explanation. One explanation is that chronic use can adversely impact social/interpersonal relationships. Goldstein's 1985 tripartite model of drugs and violence included two aspects that relate to the social/interpersonal context of use or acquisition. First, the economic compulsive model reflected criminal violence that drug users perpetrate in order to obtain money to acquire drugs. Second, the systemic violence model encompassed violence that was part of the distribution of illegal drugs, including behavior such as turf wars and retribution for inferior drugs or for informing to the police. While such models do not specifically apply to partner violence, the social/interpersonal context of use may be relevant. For example, certain patterns of use may affect interpersonal conflict and thereby increase the probability of partner violence. Homish and Leonard (2006) found that discrepant patterns of heavy alcohol use were longitudinally predictive of declines in marital satisfaction. In addition, they found (2005) that couples that drank heavily apart from each other had lower marital satisfaction than those who drank heavily together. Similar findings have been reported for substance use (Fals-Stewart, Birchler, & O'Farrell, 1999). Also partner violence may be affected by exposure to violent models of behavior. The acquisition and use of alcohol/substances most likely brings an individual in touch with violent individuals, and possibly this exposure reinforces normative acceptance of violent behavior and reduces inhibitions against behaving aggressively. Although the theoretical foundation for this possibility is very strong, research had not addressed it as of 2008.

Acute Use Explanations

Substance Expectancies. One general explanation linking alcohol and violence invokes the idea of alcohol expectancies, suggesting that individuals become aggressive while drinking because they expect that aggression is an outcome of drinking. One theme common in the literature is that alcohol results in violence because individuals believe that they can use it as an excuse to behave aggressively and to mitigate their responsibility and punishment. Quigley and Leonard (2006) described three basic questions arising from this approach. The first question is: "Do individuals believe alcohol causes people to become aggressive?" The evidence indicates that individuals do believe alcohol causes people to become aggressive, and they believe it has that effect on others much more so than on themselves (Paglia & Room, 1999).

The second basic question is: "Do people view intoxication as a mitigating circumstance in blame and responsibility attributions for partner violence?" While Richardson and Campbell (1980) found that an intoxicated man was assigned less blame than a sober man, Leigh and Aramburu (1994) reported that the intoxicated man received more blame, and Dent and Arias (1990) found no effect of intoxication on the blame assigned to the man. While these studies have focused on college students, other studies of social workers (Home, 1994), police officers (Stewart & Maddren, 1997), and couples who have experienced domestic violence suggest that alcohol does not serve as a mitigating factor. Moreover, in the area of domestic violence, evidence with respect to actual behaviors suggests that alcohol does not usually mitigate responsibility or the likelihood or severity of punishment for violent behavior. Thompson and Kingree (2006) found that alcohol use in a violent event was associated with an increased likelihood of reporting the event to the police. Other studies have found that intoxicated aggressors are more likely to be arrested than sober aggressors (Hoyle, 1998), although some studies have not found any impact of alcohol involvement on the likelihood of arrest (Robinson & Chandek, 2000). Finally, with respect to actual punishment, Harrel (1981) used characteristics of 628 pre-sentence reports to predict severity of sentence received by the offender. Alcohol use resulted in a less severe sentence for the low severity crimes but was associated with a more severe sentence for high severity crime.

The third question is: "Does possession of an alcohol-aggression expectancy predict the occurrence of partner violence?" Although some surveys have

found this relationship (Barnwell et al., 2006), the one longitudinal study (Leonard & Quigley, 1999) did not find that expectancies regarding alcohol and aggression were predictive of later partner violence. One implication of the excuse position is a placebo beverage should result in increased aggression. The two studies assessing the effect of a placebo on marital behaviors found that whereas alcohol reliably increased verbalizations that might lead to partner violence, the placebo beverage did not, a finding that is consistent with the meta-analyses of laboratory studies of alcohol and aggression conducted by Bushman and Cooper (1990).

Psychopharmacological Effects. The second broad class of models focuses on the psychopharmacological impact of the various substances. While studies of illicit drugs and violence often invoke such explanation, focusing on arousal, reduced anxiety, or altered perceptions, research has not systematically examined these explanations. Regarding alcohol, as of 2008 the focus has been on alcohol's ability to disrupt cognitive processes (e.g., Taylor & Leonard 1983; Steele & Josephs, 1990). Alcohol is generally believed to impair cognitive processes that under normal circumstances would inhibit aggressive responding. Alcohol weakens inhibitions and allows for dominant cues and dominant response options to those cues to determine behavior. Accordingly, alcohol should have more effect on individuals with already somewhat compromised attentional and appraisal abilities and on individuals with aggressive perceptual and behavioral propensities. Much research on the alcohol/aggression relationship agrees. Specifically, evidence suggests that individuals with attentional/behavioral tendencies that are facilitative of aggression are more aggressive with alcohol, whereas individuals with tendencies that are not facilitative of aggression are not more aggressive with alcohol (or are less so).

ASSOCIATION BETWEEN CHRONIC SUBSTANCE USE/ABUSE AND INTIMATE PARTNER VIOLENCE

Cross-sectional Studies. Although there are occasional disconfirming reports, excessive alcohol use by men is consistently associated with partner violence by men, including several studies of nationally representative samples. For example, the 1975 and 1985 National Family Violence Surveys found that drinking patterns in men were consistently related to marital violence (Kaufman Kantor & Straus, 1989). With over two thousand men in this study, this was one of the largest, most comprehensive studies of the issue. Studies designed to examine the association between alcohol and partner violence in nationally representative samples of specific ethnic subgroups have found some variation in the strength of the association among European Americans, African Americans, and Hispanic Americans (Caetano et al., 2001). Similarly, diversity in the strength of the alcohol/violence relationship exists among Hispanic Americans from different countries of origin (Kaufman Kantor, 1997).

In addition to general population samples, research has documented the alcohol/violence relationship in a variety of more select populations. For example, Leonard and associates (1985) evaluated 352 married, blue-collar workers, and found that men with a current diagnosis of alcohol abuse or dependence had higher rates of marital aggression (50% and 39%, respectively) than men with no diagnosis (15%) or a past diagnosis of abuse (8%) or dependence (18%), suggesting the importance of current alcohol use. Among samples seeking health care, a relationship between partner drinking and partner violence has been observed in samples based in emergency rooms (Kyriacou et al., 1998), primary health care settings (McCauley et al., 1995), family practice clinics (Oriel & Fleming, 1998), prenatal clinics (Muhajarine & D'Arcy, 1999), and rural health clinics (Van Hightower & Gorton, 1998).

Studies of samples selected specifically because of violent behavior or heavy drinking have also generally supported a relationship between heavy alcohol use and violence. For example, with few exceptions, men in treatment for partner abuse have higher rates of alcohol problems in contrast to appropriate comparison samples (e.g., Barnett & Fagan, 1993). Similarly, men seeking treatment for alcoholism manifest higher rates of domestic violence than do comparison groups drawn from the general population (O'Farrell & Murphy, 1995).

While studies focused on partner violence by males have consistently found that excessive drinking is associated with partner violence, the situation is

more complex with respect to women's drinking. Early research focused on whether female victims of domestic violence manifest patterns of heavy and problem drinking. For example, the association has been observed among women in primary care settings (McCauley et al., 1995), prenatal clinics (Stewart & Cecutti, 1993), emergency rooms (Roberts et al., 1997), alcohol treatment (Miller et al., 1989), and in the general population (Kaufman Kantor & Asdigian, 1997). These findings are complicated by two factors. First, given the association between women and men's drinking, studies that control for men's drinking are the most pertinent. Across community samples, several studies failed to find a relationship between women's drinking and IPV after controlling for men's drinking (Kaufman Kantor & Asdigian, 1997; Leonard & Senchak, 1996) possibly because of the small number of very heavy-drinking women. Other studies found a relationship (Schafer et al., 2004). Second, given the many couples in which both members of the couple are aggressive, this finding might reflect an association between the woman's alcohol use and her own aggression. For example, Schafer and associates (2004) interviewed approximately 1,600 European American, African American, and Hispanic couples in 1995 and interviewed them again in 2000. For both European American and African American couples, men's alcohol problems were associated with male-to-female violence, and female alcohol problems were associated with female-to-male violence. Studies of clinical samples of alcoholic or violent women are strongly supportive of a relationship. Similar to the findings of Schafer and associates (2004), Stuart and colleagues (2006) studied men and women arrested for IPV and found that perpetrators' alcohol problems were associated with their frequency of IPV, and the partners' alcohol problems were associated with the frequency of their IPV toward the identified perpetrator, for both male and female perpetrators.

Although research addressing women's drinking has usually controlled for the effects of partner's drinking, two studies suggested that the configuration of couple's drinking patterns may be important predictors of IPV. Quigley and Leonard (2000) found that husband and wife excessive drinking in the first year of marriage interacted to prospectively predict violence over the subsequent two years. The interaction indicated that IPV was more likely for excessive-drinking husbands with light-drinking wives. Leadley and associates (2000) found that discrepant drinking patterns were associated with IPV after controlling for heavy drinking. Perhaps excessive drinking is not as contentious when both partners are heavy drinkers as it is when only one partner is.

Fewer studies have focused on chronic drug use than on chronic alcohol use. In general, findings from both clinical samples (e.g., Moore & Stuart, 2004) and epidemiological samples (e.g., Cunradi et al., 2002) have found a relationship between drug use and intimate partner violence. However, many individuals who use illicit drugs also use alcohol excessively and have partners who do likewise. These individuals are more likely to display other characteristics of antisocial personality. When these factors are controlled in multivariate analyses, the relationship between an individual's illicit drug use and partner violence is not uniformly significant, which may reflect issues of statistical power. In a study with a larger sample of abused women (N=427) (Walton-Moss et al., 2005), neither women's alcohol nor drug use differed significantly between abused women and controls in multivariate analyses. However, there was more male drug and alcohol use among the partners of these abused women than the control women in these analyses.

Meta-analyses. The results of these case-control and cross-sectional studies are consistent. Lipsey and associates (1997) conducted a meta-analysis examining thirty-four studies of chronic alcohol use and domestic violence. These meta-analyses studies combine information from many studies to provide a statistical summary of a key set of results that may not be able to be assessed in any single study. Overall, the results showed a significant association between chronic alcohol use and domestic violence. Additionally, Stith and colleagues (2004) conducted a meta-analysis and found that both alcohol use and illicit drug use were predictors of male violence toward partners. Women's alcohol use was a significant predictor of female violence toward their partners; however, there were an insufficient number of studies that assessed women's illicit drug use to examine this issue in the meta-analysis.

Longitudinal Studies. Finally, some longitudinal evidence exists for a relationship between alcohol/substance use and intimate partner violence, although most of the research has focused on alcohol, and on male partner violence. Two of these studies focused on newlywed couples. Heyman and associates (1995) assessed couples prior to marriage and found that scores on the Michigan Alcoholism Screening Test were associated with serious aggression at the six-month assessment, but not at the eighteen- or thirty-month assessment. Leonard and Senchak (1996) also assessed couples at the time of marriage and found that scores on the Alcohol Dependence Scale were predictive of the frequency of marital aggression reported at the first anniversary after controlling for premarital aggression, perceived relationship power, perceived conflict behavior, hostility, gender identity, and history of family violence. Quigley and Leonard (1999) extended this follow-up to the third anniversary and found that husband's alcohol use was predictive of subsequent marital aggression, but only among couples in which the wife was a light drinker.

Two longitudinal studies have examined alcohol use/problems and intimate partner violence over longer time frames, such as three to six years (Caetano et al., 2005; Mihalic & Elliot, 1997). The findings from these studies support a univariate relationship between alcohol problems and partner violence, but when other factors are controlled in the analysis, the relationship is less consistent.

International Studies. A growing international literature documents that individuals who have engaged in intimate partner violence are more likely to use alcohol and other substances or to use them excessively than are individuals who have not engaged in partner violence. Much of this research focused on men's violence against women and did not examine women's violence. A 2002 WHO Report of Violence (Krug et al., 2002) notes that "population-based surveys from Brazil, Cambodia, Canada, Chile, Colombia, Costa Rica, El Salvador, India, Indonesia, South Africa, Spain, and Venezuela also found a relationship between a woman's risk of suffering violence and her partner's drinking habits" (p. 98). In 2004, Kishor and Johnson reported a multi-country study based on the Demographic and Health Surveys program, a nationally representative survey of households. By 2003, eleven countries had collected data from women with respect to domestic violence, although not all of these countries collected data concerning the husband's or partner's alcohol use. In every country in which both domestic violence and partner alcohol use were assessed, there was a significant relationship. These countries were Cambodia, Colombia, Dominican Republic, Haiti, Nicaragua, and Peru. Other studies reported the association among 170 women in poor villages in rural India (Rao, 1997), approximately 1,100 women in northwest Ethiopia (Yigzaw et al., 2004), and among 1,300 randomly selected women in three provinces in South Africa (Jewkes et al., 2002). None of these studies assessed substance use other than alcohol.

Moderators of the Chronic Association. Clearly, no one-to-one relationship exists between chronic heavy drinking or substance use and intimate partner violence. Instead, association is limited to certain people under certain circumstances. Only a few studies have provided evidence addressing this issue, and these are exclusively focused on alcohol use and male partner violence. The most consistent moderator appears to be the presence of other factors that are causally implicated in partner violence. For example, several studies found that heavy drinking is associated with marital violence only among hostile (Leonard & Blane, 1992) or discordant married couples (Leonard & Blane, 1992; Margolin et al., 1998). Evidence shows that alcohol is associated with marital violence in the presence of high levels of negative affect (Leonard & Blane, 1992) and stressful life events (Margolin et al., 1998). Factors that moderate the longitudinal relationship between heavy drinking and marital violence were examined by Quigley and Leonard (1999). This analysis focused on verbally aggressive conflict, a variable that reflects hostility and marital dissatisfaction. This study demonstrated that heavy drinking predicted subsequent aggression only among couples high in verbally aggressive conflict styles.

ASSOCIATION BETWEEN ACUTE ALCOHOL/SUBSTANCE USE AND INTIMATE PARTNER VIOLENCE

It is important to distinguish between alcohol and substance use as chronic variables describing an individuals' usual use and acute substance use that occurs in temporal proximity and prior to the

occurrence of partner violence. A number of studies have focused on acute consumption as a predictor of partner violence. The vast majority of this research is concerned with alcohol use.

Event-based Survey Research. Studies of violent events involving intimate partners often report that one or both members of the couple were using substances (usually alcohol) prior to the occurrence of violence. However, these reports, by themselves, are not informative regarding the potential causal role of alcohol or other substances on the occurrence of violence. They become informative when comparisons can be made to the presence of these substances in control events. To this end, researchers have adopted one of two basic strategies, a between-subjects approach and a within-subjects approach.

In the between-subjects approach, individuals who experienced a violent event are compared to different individuals who experienced only a control event, such as verbal conflict, with respect to the characteristics of the event. Several studies in community samples have compared violent events with control events and found that heavy drinking, at least by the male, was more common in violent than in control events (Leonard & Quigley, 1999). McClelland and Teplin (2001) reported on over 1,200 police-citizen encounters and using a validated observational checklist of alcohol found spousal assault encounters were more than twice as likely to involve alcohol as nonviolent encounters. Campbell and associates (2003), in univariate analyses, found a higher incidence of alcohol and drug use prior to femicide in contrast with nonlethal abuse of women. However, this effect was not significant in the multivariate analyses, possibly because it was mediated by other event-level characteristics, such as using a gun.

The second approach to event-level studies, the within-subjects approach, focuses on individuals who have experienced both a violent event and a control event or events, and compares the characteristics of the two. Several studies using this within-subjects approach suggest that acute alcohol use is associated with the occurrence (Leonard & Quigley, 1999) or severity of partner aggression (Wells & Graham, 2003). Studies of couples in treatment for alcoholism (Murphy et al., 2005) and domestic violence (Fals-Stewart, 2003) have reported similar findings.

Only two studies as of 2008 have used an event-based approach to examine the impact of illicit substances of the occurrence of partner violence. Murphy and associates (2005) found that violent events were more likely to involve heavy drinking by both husbands and wives than were control conflict events but that the use of other drugs was comparable across the two events. In contrast, Fals-Stewart and colleagues (2003) collected daily diary data concerning partner violence and substance use from men entering substance abuse treatment and from their partner for fifteen months. Controlling for marital adjustment and antisocial personality, the use of either alcohol or cocaine on a given day significantly increased the likelihood of severe violence on that day.

Experimental Studies of Alcohol and Aversive Verbal Behaviors. In various experimental studies, primarily focused on young men, participants were randomly assigned to receive alcohol or to receive no alcohol or a placebo and then given the opportunity to administer an aversive stimulus to another person usually another male. Several meta-analytic studies (Bushman & Cooper, 1990; Lipsey et al., 1997) confirmed that participants who received alcohol selected more aggressive responses than participants who received either no alcohol or a placebo. However, the relevance of these findings to partner violence was uncertain.

Other experimental studies have examined whether alcohol consumption affects verbal behaviors that might be related to the occurrence of partner violence, particularly within the context of relationships. In these studies, couples were asked to discuss and attempt to resolve potential or actual relationship conflicts. The interactions were videotaped and rated with respect to the behaviors displayed, including verbally aggressive behaviors. Two major projects used the conflict resolution paradigm to study the impact of alcohol on negative verbal behaviors. The first of these, conducted by Jacob and colleagues (Haber & Jacob, 1997; Jacob & Krahn, 1988) involved couples in which the husband or wife was alcoholic or depressed or had no diagnosis. These couples and a teenage child participated in a series of family interactions on two nights, one in which the adults were provided access to their usual alcoholic beverages (alcohol session), and one in which the adults were

provided nonalcoholic beverages (no alcohol session). Jacob and Krahn (1988) found that only couples in which the husband was alcoholic tended to display higher levels of negativity during the alcohol session versus the no alcohol session. Haber and Jacob (1997) used the same sample but included couples in which the wife was alcoholic. They specifically compared couples in which husband, wife, both, or neither was alcoholic and found a general increase in negativity from no alcohol to alcohol sessions, except among couples in which only the wife was alcoholic. In the second research project, Leonard and Roberts (1998) allowed couples to discuss a marital conflict under a baseline condition. They were then randomly assigned to one of three conditions: no alcohol, husband placebo, or husband alcohol. Men who received alcohol displayed higher levels of negativity than men in the placebo or no alcohol condition, as did their wives who did not receive alcohol. Although couples that had experienced husband-to-wife aggression engaged in higher levels of negativity, they were not differentially impacted by the alcohol administration. Thus, these two studies demonstrate that alcohol can increase negative relationship behaviors, although whether this increase is specific to alcoholic couples or is applicable to other types of couples is uncertain.

The role of alcohol in aversive verbal expressions was examined by Eckhardt (2007). In this study, maritally violent and nonviolent men were randomly assigned to receive alcohol, placebo, or no alcohol. They then heard brief descriptions of anger-arousing situations, imagined that they were in the situation, and spoke out loud about their thoughts and feelings. They were tape-recorded and their thoughts and feelings were coded. Although ratings of anger were not affected by alcohol, alcohol led to an increase in aggressive verbalizations for maritally violent men, but not for nonaggressive men. Similarly to Leonard and Roberts (1998), the placebo did not influence anger or aversive verbalizations for either group.

Some evidence indicates that individuals with hostile/antisocial tendencies are most responsive to alcohol. In studies described above by Jacob and colleagues, Jacob, Leonard, and Haber (2001) found that among couples with an alcoholic husband, the increase in negativity from the no alcohol to alcohol session was only observed in couples in which the husband was also antisocial. In Eckhardt's 2007 study, alcohol administration resulted in the highest level of aggressive verbal statements among men who scored high with respect to their typical level of anger. Finally, at the daily level, Fals-Stewart and colleagues (2005) found that alcohol use on a specific day increased the probability that severe aggression would also occur on that day and that this effect was the strongest among men with an antisocial personality disorder.

IMPACT OF ALCOHOL/SUBSTANCE ABUSE TREATMENT ON PARTNER VIOLENCE

If substance use, particularly acute substance use, is causally related to the occurrence of partner violence, the cessation of substance use should lead to reductions in partner violence, which is particularly relevant for individuals in treatment for substance abuse. Several studies have found that individual treatment of alcoholism leads to reductions in partner violence (Stuart et al., 2003), an effect that is observed among those alcoholics who have not relapsed (O'Farrell et al., 2003).

Although marital therapy is often viewed as inappropriate for couples in which the husband has engaged in violence, combined behavior marital therapy and alcoholism treatment developed as an efficacious treatment for alcoholism prior to recognition that many of the alcoholics had engaged in partner violence. As a result, considerable research demonstrates that alcoholic behavioral couples' therapy results in reduced alcohol involvement and in reductions in partner violence, that this reduction is also apparent for verbal aggression, and that this reduction is observable up to two years post-treatment (O'Farrell et al., 2003). In addition, O'Farrell and associates (2004) found that the extent to which a couple was actively engaged in behavioral couples' treatment (BCT) was predictive of post-treatment partner violence in alcoholic men, and mediation analyses suggested this occurred because treatment involvement led to improved relationship functioning and reduced drinking.

Although evidence shows that the successful treatment of men seeking alcoholism treatment is associated with reductions in marital violence, it is unclear whether alcoholism or substance abuse treatment of violent men identified in the criminal

justice system would have the same effect. Murphy and associates (1998) contrasted partner violent recidivists with nonrecidivists with respect to the different judicial and other interventions to which they were mandated. These groups did not differ with respect to referral to alcohol/drug counseling; however, it is unclear whether all of the participants needed alcohol/drug counseling. A similar analysis was undertaken by Babcock and Steiner (1999). In this study, successful completion of a chemical dependency program was associated with a reduced risk of recidivism, but this was not significant when the analyses controlled for previous criminal record and the number of domestic violence treatment sessions attended. However, neither of these studies was a randomized clinical trial that examined adding alcohol treatment to the other treatments administered to batterers, and neither assessed whether the offender remained in remission, a critical issue in the alcoholism treatment literature. As of 2008, it remained unclear whether treatment for substance abuse among men in the criminal justice system has any added impact on domestic violence beyond the other conditions imposed in that system.

See also **Alcohol; Child Abuse and Drugs; Cocaine; Treatment, Behavioral Approaches to: Couples and Family Therapy.**

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IRELAND, REPUBLIC OF. Stereotypes of the Irish as heavy drinkers have had international currency for centuries, but the main aim of this entry is to review drinking habits in the Republic of Ireland against the more recent historic background of economic affluence. In addition to this focus on alcohol, the entry will also look at the relatively new phenomenon of illicit drug use, as well as at policy attempts to reduce the harm associated with tobacco use in this country.

ALCOHOL

The Irish, it would appear, have always enjoyed alcohol, and the coming of Christianity to Ireland in the fifth century did not alter attitudes toward a substance regarded as one of life's great boons. A poem attributed to Saint Bridget, an early Christian saint, describes heaven as a lake of beer around which the heavenly family sits drinking for all eternity. Following the introduction of distillation to Ireland (probably in the fourteenth century), it is possible to trace the emergence of a somewhat different discourse, one that views alcohol consumption as problematic and suggests that the Irish are distinguished by an inability to control their drinking. However, historic portrayals of the "drunken Irish" must be interpreted cautiously, because from the 16th century onward, when the English colonization of Ireland became more systematic, such portrayals formed part of a wider English critique of the Irish, as well as serving as a legitimation of the "civilizing" role of the English in this subject nation.

Early Temperance Efforts. Concerns about excessive drinking came to a head immediately before the catastrophic potato famine of the 1840s, when a Catholic priest, Father Theobald Mathew, initiated a religious temperance movement that persuaded about half of the adult population to take a pledge of total abstinence. A detailed study of this movement titled *Ireland Sober, Ireland Free* (1986), Elizabeth Malcolm reveals that there was a wide range of motivations on the part of those who espoused temperance. Malcolm also highlights the ambivalence of the Catholic bishops toward a movement that was suspiciously Protestant in its denunciation of alcohol.

After the death of Father Mathew—whose leadership was charismatic in style, and who left behind no organizational structures to continue his work—the Irish population appears to have drifted back to its previous drinking habits, and it was not until 1898 that the Pioneer Total Abstinence Association of the Sacred Heart was established under the control of the Catholic hierarchy in Ireland. This mainstream Catholic movement, which still survives (albeit with a limited membership), was more moderate ideologically than Father Mathew, in that it did not view alcohol as inherently evil, but merely regarded abstinence as

a voluntary sacrifice that some Catholics might undertake for religious motives.

In 1922, twenty-six of the country's thirty-two counties achieved self-government, and in 1949 they left the British Commonwealth and declared a republic. In 1973 the Republic of Ireland joined what is now the European Union (EU). Although there were periodic expressions of concern at the damage that alcohol consumption was causing to Irish society, it is clear in retrospect that consumption levels were low for the first forty years of self-government, as was the prevalence of alcohol-related problems. In 1950, for example, annual alcohol consumption per adult (age 15 and over) was just 4.67 liters, and this figure rose only slightly (to 4.80 liters) over the next 10 years (Walsh, 1983).

During this period, Catholic temperance was still strong and the influence of the Catholic Church on public alcohol policy was evident in the restricted opening hours of pubs and the policy of no "Sunday opening" in most parts of the country. Following a liberalization of opening hours in 1960 and a marked decline in temperance sentiment, consumption levels crept up gradually, but the most dramatic increases in Irish alcohol consumption have occurred during the years of economic affluence, which began in the early 1990s and are known colloquially as the "Celtic Tiger" era.

A Growing Problem and New Strategies. Changes in drinking levels, patterns, and related problems were documented in a 2002 report of the Department of Health and Children titled *Strategic Task Force on Alcohol: Interim Report* According to this report, "between 1989 and 1999, alcohol consumption per capita in Ireland increased by 41 percent while ten of the European Union Member States showed a decrease and three other countries showed a modest increase during the same period." More recent comparative data for the year 2003 show that, at 13.4 liters per year, adult alcohol consumption in Ireland was third highest for the enlarged EU, which now consists of 26 countries (Hope, 2007). Researchers have also gathered detailed epidemiological data showing that Irish drinking patterns are distinctively problematic—specifically the habit of heavy episodic, or "binge," drinking—and that there have been increases in a range of health and social problems associated with alcohol consumption.

Since the mid-1990s, there has been an almost continuous policy debate on the topic of alcohol and its negative impact on Irish society. Public policy on this issue, however, continues to be marked by ideological conflict and administrative fragmentation. In 1946, Ireland was the first European country to have a branch of Alcoholics Anonymous, and over the next twenty years—largely through the promotional work of the World Health Organization (WHO)—the disease concept of alcoholism gained official acceptance within Irish health policy. The WHO did an about-face on this matter during the 1970s, and a public health, or "total consumption," model of alcohol problems emerged. Unlike the disease concept, which largely attributed alcohol-related problems to the vulnerabilities of a small minority of "diseased" consumers, the public health model emphasized the negative features of alcohol per se, and argued that the prevalence of alcohol-related problems would only be reduced by control policies aimed at reducing societal consumption levels. Since then, public health researchers and advocates have repeatedly recommended that this model should underpin public policy on alcohol in Ireland. Specifically, they argue there should be an integrated national alcohol policy based on the use of evidence-based prevention strategies.

The *Strategic Task Force on Alcohol: Second Report*, released in 2004, recommended that the first objective of such a national alcohol policy should be to reduce Irish consumption to the EU average of 9 liters per annum. In pursuit of this objective, the report recommended that the state should increase the excise duty on alcohol and restrict its physical availability by reducing both the number of retail outlets and the hours of sale. It also suggested that the government control the ways that the drinks industry advertises and promotes its products. These recommendations reflect the new WHO position that alcohol is "no ordinary commodity," but they are in ideological conflict with the neoliberal values currently dominant in Ireland. To date, therefore, the government has been reluctant to implement strategies that would both bring it into direct conflict with the drinks industry and be electorally unpopular.

ILLICIT DRUG USE

In Ireland, public concern and policy in relation to illicit psychoactive drugs dates back to the mid-1960s. The first modern antidrug legislation in the country was the 1977 Misuse of Drugs Act. In retrospect, these early concerns appear exaggerated, for the prevalence of illicit drug use was low, the drugs being used were relatively "soft," and there was little or no injecting of these drugs. Things changed in 1979, when—in what came to be known as the "opiate epidemic"—working-class areas of Dublin experienced a dramatic and sustained wave of injecting heroin use. This upsurge was accompanied by the usual range of health consequences—dependency, overdoses, and the physical complications of sharing needles—as well as increases in acquisitive crime and other social problems in the affected areas (Butler, 2002).

Public policy and service provision struggled to adapt to the opiate epidemic, a task that was further complicated by the advent of HIV/AIDS and the early recognition of the fact that needle-sharing among injecting drug users played a major role in the transmission of this new virus. Prior to the coming of HIV/AIDS, it had been assumed axiomatically that all health-service responses to illicit drug use would have abstinence as their goal, thereby ensuring that treatment and rehabilitation professionals worked collaboratively with colleagues from the criminal justice system in common pursuit of the ideal of a "drug-free" society. In fact, from the late 1980s onward, both statutory and voluntary treatment agencies shifted incrementally to the use of harm-reduction models of service provision, which included methadone maintenance, needle and syringe exchange, the use of mobile clinics, and the introduction of "low-threshold" agencies and outreach work for problem drug users who were uncommitted to any major lifestyle change.

The adoption of such harm-reduction strategies clearly marked a decline in the influence of American methods. Instead, Irish policymakers and service providers drew on the experiences of countries such as Holland, which had previously adopted a more pragmatic approach to managing drug problems, and which clearly had no faith in the approach being used in the so-called War on Drugs in the United States (Butler and Mayock, 2005). In 1993 the EU-established European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and Ireland's Health Research Board became a national data-gathering "focal point" for this effort. This development further reinforced the tendency for Irish policymakers to look to Europe rather than the United States for guiding influences.

A New Approach. Following recommendations made in the *First Report of the Ministerial Task Force on Measures to Reduce the Demand for Drugs*, issued by the Department of the Taoiseach (prime minister) in 1996, a new managerial approach was taken to drug policymaking. This effort involved the creation of a system of a multilayered policy and administrative structures, including both top-down and bottom-up initiatives. An explicit aim of this effort has been to create a "cross-cutting" response to illicit drugs, in which all central government departments and agencies coordinate their activities to ensure that, as far as possible, there are no philosophical or practical conflicts between different sectors of government. This approach to policymaking was formalized in a policy review titled *Building on Experience: National Drugs Strategy 2001–2008*, which was based on four "pillars": supply reduction, prevention (i.e., education and awareness raising), treatment, and research. It also laid out detailed objectives, as well as specified actions deemed necessary to attain these objectives, and it identified the agencies that would be accountable for these actions.

There is no simple way to determine whether the National Drugs Strategy has been a success. The primary impetus for the creation of the strategy was the necessity to respond to heroin problems in readily identifiable urban areas. Through its community-based structures, the effort could be deemed to be successful in this sphere. However, on the broader front of preventing recreational drug use among adolescents and young adults, the strategy has clearly not made much impact. For instance, the 2003 report of the European School Survey Project on Alcohol and Other Drugs (ESPAD), a comparative study of drug and alcohol use among 16-year-olds in 35 European countries, showed the Irish sharing third place for lifetime prevalence of cannabis use. It was also the leading nation in binge drinking.

One of the unanticipated consequences of the creation of the National Drugs Strategy has been the way in which it has highlighted the absence of any similar strategy to deal with alcohol, prompting suggestions both from community groups and political leaders that the existing strategy should be expanded to include alcohol. In management terms, this is commonly spoken of as creating "synergies," but in political terms it is obviously a move that would be resisted strongly by the country's powerful drinks industry.

TOBACCO

Given the tendency of the Irish to indulge heavily in the use of psychoactive substances, it might come as a surprise that Ireland has led the EU in tobacco control efforts. Public health advocates had conducted a long campaign for legislative control of smoking in public places, culminating in the Public Health (Tobacco) Act of 2002, which established an Office of Tobacco Control (OTC). Despite intensive lobbying from the tobacco and hospitality industries, the OTC persuaded the Minister for Health and Children to introduce national regulations prohibiting smoking in all workplaces, and these regulations came into effect in March 2004. Much of the publicity surrounding this development focused on the fact that smoking was being banned in pubs, and it was commonly predicted that such a ban would be unenforceable. In fact, the ban was publicly accepted and has been successfully enforced, thereby offering protection from secondhand smoke to workers and demonstrating that public health activists could successfully counter the influence of powerful commercial interests.

See also **Alcohol: History of Drinking; Crime and Alcohol; Crime and Drugs; European Union; Foreign Policy and Drugs, United States; Harm Reduction; International Drug Supply Systems; Needle and Syringe Exchanges and HIV/AIDS; Tobacco: An International Overview.**

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SHANE BUTLER

ITALY. The European Addiction Monitoring Centre has estimated that in the European Union approximately 50 million people out of the total European population of 490,426,060 have tried an illegal substance in their lifetime, and at least 7 percent of these subjects, ranging from 15 to 64 years of age, have done so recently. According to a 2004 report on drug addiction prepared by the Italian Parliament, at least 20 percent of the Italian population ranging from 15 to 54 years of age have tried an illegal substance at least once in their lives and this percentage is even higher, 30 percent, for those 15 to 34 years old. A distinction must be made between recreational drug users and drug addicts, who are estimated to represent less than 1 percent of the total Italian population and the majority of whom are assisted by public health and welfare services.

EPIDEMIOLOGY

In Italy, the impact of illicit drugs was first felt on a broad scale during the mid-1960s. The patterns in Italy were similar to those observed in other European nations. These models seemed to be associated with young people's rejection of the existing political and social order. Opioids, especially heroin, began to be used illicitly, and by the 1970s serious consequences ensued. By then, the countercultural movement and its abuse of illicit drugs had veered from most of its original idealistic principles. Abusers were simply in search of ever more and ever stronger psychotropic effects. Moreover, criminal organizations took charge of the illicit drug trade, not only to increase their profits but also to control and direct the political and social development of the youth of Italy. For the most part, users became abusers who were physically dependent on their drug of choice, so their behavior could be controlled by suppliers.

In the 1980s the drug scene changed, with various control measures enacted by the government and less heroin available on the street. In addition, with less heroin being sold, longer intervals occurred between drug doses for many users. Such modified habits led to decreased tolerance and increased overdosing, with many deaths resulting. For these reasons, the number of heroin addicts in Italy decreased, but in the mid-1980s the illicit use of cocaine emerged as the new drug problem. Its crack and freebase forms were especially harmful among young adolescents. After a modest decrease in heroin consumption in the late 1990s, its further increase was recorded in the early twenty-first century, with cocaine use steadily increasing during the 1990s and first few years of the new millennium. The mode of administration of these drugs also varied—although injection rather than smoking and snorting became common for both heroin and cocaine. In particular, approximately 70 percent of patients treated in the Centers for Addiction Treatment (CATs) admitted heroin use (70% injected it) and 16 percent cocaine use (8% injected it) as the primary substance of abuse.

One interesting study (Zuccato et al., 2005) has also shown that cocaine is present and measurable in surface waters of populated areas. The largest Italian river, the Po, with a 5-million-people catchment's basin, steadily carries the equivalent of about 4 kilograms of cocaine per day. This implies the average daily use of at least 27 +/- 5 doses, of 100 milligrams each, for every 1,000 young adults, an estimate that greatly exceeds official national figures. In this same study, the researchers used the environmental cocaine levels for estimating collective consumption of the drug, an approach with the unique potential ability to monitor local drug abuse trends in real time, while preserving the anonymity of individuals.

In recent years approximately 10 percent of patients seen at CATs identified cannabis as their primary substance of abuse and, compared to other addicted patients, these individuals presented a lower mean age, 19 years.

Another recent survey (Pavarin, 2006), this one conducted in the northern part of Italy, investigated drug use among more than 2,000 youngsters attending open-air musical events—so-called street raves. It confirmed the high prevalence of hashish, marijuana, and cocaine use and a drop in the average age of first-time use, 16 years. In addition, in the years since 2001 several new drugs emerged as specifically consumed by young people. The most commonly used new substances were first salvia divinorum—a psychedelic drug—followed by hallucinogenic mushrooms and 3,4-methylenedioxymethamphetamine (MDMA), commonly known as Ecstasy, poppers, and ketamine. Clear evidence also emerged regarding the potential risks associated with current changes in drinking patterns among youth who are decidedly *buzz-oriented* as well as the high prevalence of risk behaviors, such as the use of mixtures of drugs on the same evening, combining of alcohol consumption with drugs, and driving after drinking.

In regard to the so-called legal drugs, alcohol, and tobacco, in 2007 the Institute of Health estimated that approximately 30 percent of the Italian population—mostly men—smoke tobacco on a daily basis. About 20 percent of these smokers are very young—from 15 to 24 years old—and 8 percent smoke more than 25 cigarettes per day. However, there is evidence that tobacco consumption progressively decreased from 1957 to 2007; in particular, a relevant reduction of 0.8 percent occurred from 2001 to 2007 and the mean number of cigarettes

consumed also declined from 16.8 per day in 2001 to 14.1 per day in 2007.

Alcohol use in Italy strongly differs from drug use for historical, traditional, behavioral, and cultural reasons; supply and distribution are also different, because alcohol is free from legal restrictions. Wine is the most frequently used alcoholic beverage. Although wine consumption was gradually displaced during the 1980s with the substitution of other liquors and beers, the total amount of alcohol consumed remained almost constant. Among the 70 percent of Italians who admit consuming alcohol, not quite 70 percent of them consume one or more standard drinks occasionally—one standard drink corresponds to about 14 grams of pure alcohol—and approximately 30 percent report daily alcohol intake.

In addition, from 1995 to 2007 drinking habits also changed; this phenomenon was particularly evident among the young. The so-called Mediterranean habit of drinking alcohol or wine during meals acquired by older generations of farmers has became less popular; conversely, the so-called Anglo-Saxon practice of *binge drinking*—drinking spirits and beer outside meal times to get high or to achieve a state of drunkenness—has been progressively favored by the younger segment of the population. About 8 percent of them describe themselves as binge drinkers. Indeed, in Italy this phenomenon is on the rise. In addition, the age of first-time drinkers has declined to 11 years, and beer and alcoholic soda pop or wine coolers—carbonated fruit-juice-flavored beverages with a concentration of 3 to 5 percent alcohol—have become the most popular beverages among youth. An important related development is the association of illicit drug use and binge drinking with high-risk sexual behaviors. A recent multicenter survey (Bellis et al., 2008) in the city of Venice reported that recreational drug use, particularly cocaine and Ecstasy, in combination with binge drinking altered the sexual decision making of its subjects and increased their chances of engaging in unsafe and later regretted sexual activities. Substance use also appears to be an integral part of strategies for engaging in sex.

Researchers Adamo and Orsini (2007) have calculated that around 7 percent of Italians have alcohol-related problems involving high-risk use or abuse, and 3 percent are affected by alcohol dependence, which appears to be mainly a problem of chronic abuse by adults over the age of 40. However, since the mid-1980s alcohol dependence in Italy has come to include a greater number of women and young people. In same cases, alcoholism has also been complicated by the regular combining of alcohol with psychotropic drugs—that is, tranquilizers—and other substances—that is, cocaine and amphetamines—as demonstrated by the greater number of patients affected by polysubstance dependence treated in CATs.

DEATHS RELATED TO DRUG, ALCOHOL, AND TOBACCO USE

Drug-abuse-related deaths show irregular trends. Most deaths, however, may be attributed to heroin overdoses or to accidents while injecting it. After 1980 two large increases in the death rate occurred, first in 1982 and then in 1984, followed by a steady rise into 1986. From 1986 to 1988 the mortality rate nearly doubled; it subsequently remained steady until 1991 and then dropped until 1994, except among the elderly, for whom the rate increased. Since the mid-1990s the mortality rate has continued to decline. Indeed, from 1993 to 2006 the number of addicts treated in CATs increased—from 109,000 subjects in 1993 to 176,000 in 2006—and a reduction in the number of deaths from overdose was recorded—from 888 subjects in 1993 to 517 in 2006—with a corresponding drop in the mortality rate, from 0.8 to 0.3 percent. Some important factors, such as the administration of agonist or partial agonist drugs in association with counseling sessions and the distribution of informative materials in CATs, have contributed to this important result. Because intravenous drug use is a primary transmission route for HIV and other blood-borne diseases, such as Hepatitis B and C infections, prevention campaigns have also been developed. In particular, in the early twenty-first century CATs have actively distributed sterile needles and condoms, and information regarding the risky behaviors of drug addicts. As of 2008, 44 percent of the CATs in Italy distributed sterile needles and condoms, and more than 90 percent of CATs supplied information regarding the risk of infections associated with the use of illicit drugs. Moreover, CATs have devised vaccination strategies for Hepatitis B: In recent years

some 15.8 percent of patients enrolled in a rehabilitation program have been vaccinated (Ministry of Health, 2006; Ministry of Social Affairs, 2006).

It is worth noting that alcohol-impaired driving is a serious threat to the nation's health as well. Driving license regulations have, since 1988, included a test that measures the breath concentration of alcohol in drivers' blood, which must not be over 5 grams per liter (g/l), approximately that of other countries in the European community. In Italy, 30 to 50 percent of traffic accidents are related to alcohol intake, and 50 percent of those subjects who die during such crashes are under 30 years of age. The accidents may be correlated with alcohol use and abuse. In particular, one prospective study (Fabbri et al., 2002) that enrolled more than 2,000 patients admitted to an Italian emergency room for an injury sustained during a traffic accident has shown that the patient's blood alcohol concentration (BAC) was above the legal limit in 25.7 percent of the cases. Also, the number of BAC positive patients increased progressively—from 14.4 to 30.8 percent—with trauma severity, and almost 30 percent of polytraumatized patients were BAC positive. Another Italian study (Giovanardi et al., 2005) confirmed that a significant percentage of injury-producing traffic accidents involve drivers who are under the influence of drugs of abuse, alcohol, or other drugs affecting the central nervous system. Indeed, 40 percent of the study's subjects tested positive for at least one drug and/or alcohol—66 percent tested positive for a single drug, 25 percent for two drugs, and 9 percent for three or more drugs. The recent use of marijuana was determined most frequently—accounting for 19 percent of the 115 total—well surpassing alcohol (10%), amphetamines (7%), and cocaine (6%). It is worth pointing out that most of the drivers who tested positive for alcohol or other drugs were between the ages of 21 and 40.

In Italy, 80,000 subjects die every year as a consequence of tobacco smoking. From 2000 to 2007 the number of Centers for the Treatment of Tobacco Dependence increased: As of 2008, 346 such centers existed. This development is partially attributable to (1) increased awareness of the risky medical consequences of tobacco use among the population of current smokers; (2) preventive campaigns aiming to stop smoking; (3) the warning about the fatal consequences of smoking that is printed on cigarette packaging; and (4) current legislation that prohibits smoking in workplaces and public recreational spaces—that is, cafés, discotheques, pubs, and restaurants.

TREATMENT FACILITIES

As the use of illicit drugs became an ever more serious problem, the emerging need for adequate political and social interventions aimed at preventing this expanding phenomenon and treating drug-dependent individuals became urgent. In accordance with national policy guidelines, a network of facilities was established, as were various links between rehabilitation programs, law enforcement agencies, and judicial structures. This approach was worked out with overwhelming public support, the aim being to sustain every initiative to reduce the availability of and demand for drugs. Many CATs were established throughout all of Italy's regions. In the early twenty-first century a wide range of resources were available: 544 CATs and 575 residential communities and socio-rehabilitative structures—public, private, and voluntary—with most of them situated in northern Italy. Voluntary services continue to increase in importance, both in number and in regional distribution. Of the addicts served by such facilities, almost all are heroin abusers, some not yet physically dependent on the drug. The facilities provide integrated and custom-designed programs based mainly on pharmacological support. Sixty-eight percent of patients are treated with methadone, 20 percent with buprenorphine, 7 percent with naltrexone, and 2.3 percent with clonidine, in association with psycho-social supports (38%), mostly counseling (42%), and social services (41%). Although methadone remains the most frequently used drug in CATs for the treatment of heroin addiction, one contemporary Italian study showed statistically significant improvements in the rate of heroin use, psychiatric status, and quality of life between the 3rd and 12th month of treatment with both methadone and buprenorphine medications, suggesting the long-term efficacy of both these drugs in treating the symptoms of opioid addiction and improving addicts' quality of life.

In the early twenty-first century a multidisciplinary approach to the treatment of alcohol dependence, which is a combination of pharmacological treatment, psycho-social supports, self-help groups, and family interventions, has been embraced.

Because the use of gamma-hydroxybutyric acid (GHB) as a recreational drug has not spread in Italy, it is currently employed in treating alcohol dependence with encouraging results. Indeed, GHB, due to its GABA-ergic activity (which increases the available amount of GABA and typically has anti-anxiety and anti-convulsive effects) is currently used in suppressing the symptoms of alcohol withdrawal syndrome and, alone or in combination with naltrexone, it is used as an anti-craving medication in the maintenance of alcohol abstinence. With the increased use of the above-mentioned drugs, disulfiram has become less popular among physicians. Moreover, counseling and cognitive-behavioral therapy (CBT), alone or in association with the support of self-help groups such as Alcoholics Anonymous (AA), continue to play a relevant role in the treatment of alcoholism. In fact, since the mid-1990s the number of AA groups throughout Italy has risen to over 500. In addition, throughout Italy another type of self-help group, the so-called Club System for Treated Alcoholics (CTA), also exists. It was inspired by Vladimir Hudolin, a Croatian psychiatrist who, in 1960, organized rehabilitation programs for alcoholics and their families in the city of Zagreb with subsequent extensions to other parts of the former Yugoslavia. In 1992 before the start of the Balkan War, some 1,200 Clubs had been established. Afterward the phenomenon of Clubs expanded to the nearer territories of eastern and central Europe. As of 2008, there were more than 2,300 Clubs in Italy.

LEGISLATION

When drug abuse spiraled in Italy during the 1960s, the legislation in force proved to be insufficient to cope with emerging conditions; it did not take into consideration the latest political-cultural trends, scientific knowledge of the day, or the increasingly important role of public health. In 1954 the law dictated that those defendants who produced, used, or sold illicit substances had to be punished with sentences of 6 months to 7 years in jail and additional fines. New legislation in 1975 mandated increased jail time—from 1 to a maximum of 15 years—and higher fines. However, innovative elements such as no punishment for addicts found to be in possession of a moderate quantity of illicit drugs, considered to be for personal use, characterized that legislation; in addition, therapeutic interventions in specialized centers servicing those with certified illicit drug dependence were offered. The confiscated narcotics were to be carefully examined and quantified, and that information was to be considered by the courts in relationship to the physical and psychological needs of the addict. Unfortunately, this individualistic approach was poorly applied, which made the law useless. Regulations approved in 1990 improved the state's power to both take repressive action and mandate intervention, and it defined a daily mean dose to separate administrative offenses from more serious drug-related crimes. The objective was to recover and rehabilitate drug addicts. A 1993 referendum, however, repealed the prohibition on personal drug use and canceled the regulations on a daily mean dose.

In 2006 a new revision of the law was approved by the Italian Parliament. In particular, the current law clearly specifies the maximum misdemeanor amount of individual possession for each illegal drug: for example, 1 g of cannabis, 750 mg of cocaine, 1/2 g of heroin, 750 mg of Ecstasy, 500 mg of amphetamine, and 150 mg of d-lysergic acid diethylamide (LSD). Those defendants found to be in possession of the above-defined amounts are punished with *administrative sanctions*—that is, withholding of a driver's license or gun permit, or official permission to live in Italy if the individual is not an Italian citizen; these defendants may only obtain an end to such sanctions when a CAT officially certifies that they have dutifully followed a therapeutic program with positive results. Those defendants whose possession exceeds the above-mentioned quantity of illicit drugs are considered pushers and punished as criminals with *legal sanctions* from 1 to 20 years of imprisonment.

In October 2007 the law regarding alcohol and driving was modified. In fact, a suspended license for 3 to 6 months and fine from 500 to 2,000 euros are now levied on those defendants found to be driving with a BAC ranging from 0.5 to 0.8 g/l; a suspended license for 6 months to 1 year, fine from 800 to 3,200 euros, and up to 3 months of imprisonment are imposed on those defendants found to be driving with a BAC ranging from 0.9 to 1.5 g/l; a suspended license for 1 to 2 years, fine from 1,500 to 6,000 euros, and up to 6 months of imprisonment are also applied to

those defendants found to be driving with a BAC greater than 1.5 g/l. In addition, if a defendant causes a traffic accident resulting in physical injuries to others, the administrative and penal sanctions double; with the previous law, sanctions did not differ if a traffic accident had occurred. In any case, within 60 days of having a driver's license suspended and before re-obtaining it, a subject apprehended for drunk driving must undergo a medical examination that tests for the biochemical markers of alcohol abuse and a consistently positive attitude toward the responsibilities of driving. When the subject presents behavioral modification and/or alterations of biochemical parameters of alcohol abuse sufficient to arouse suspicion of alcohol-related problems, the medical commission may request a further and more specific evaluation in a CAT by a medical doctor who specializes in treating alcohol abuse.

In January 2005 the existing legislation regarding tobacco smoking was modified. The previous law of 1962 prohibited smoking in public places (that is, hospitals, cinemas, theaters). The revised law expanded the same restrictions to all closed spaces (those offering public services, workplaces, and jails) except for those not open to the public. However, with adequate ventilation and separation from nonsmokers, specific areas for smokers are permitted in public places. Smokers violating the law are subject to fines of 27.5 to 275 euros, and inspectors are assigned to enforce it; and owners of public venues found to not uphold the statute may be fined 200 to 2,000 euros. Finally, any form of advertising related to tobacco products and their sale to those younger than 16 years of age is also forbidden.

See also **Britain; European Union; France; Nordic Countries (Denmark, Finland, Iceland, Norway, and Sweden); Spain.**

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JAPAN. Japan's involvement with global narcotics traffic follows its remarkable emergence from isolated warrior society to modern world power like a secret shadow. In 1868, when Japan formally opened its doors to world trade and diplomacy, it was with the understanding that opium would not be tolerated within its borders. After 1895, as its territories expanded into the Asian continent, the problem of narcotics addiction became a burden of empire. During the 1930s and 1940s, as the nation turned to military adventure in China and the Pacific, opium, morphine, and heroin sales financed espionage and dirty tricks in an all-out war. After surrender in 1945 and continuing into the twenty-first century, Japan has reestablished its reputation for a tough, no tolerance drug policy, and yet amphetamine abuse fueled postwar economic growth. Methamphetamine use remains a problem, although it is dwarfed by the legal drugs tobacco and alcohol.

HISTORICAL BACKGROUND

According to tradition, the poppy flowers dotting fields in the countryside came to Japan with Buddhism. During the Tokugawa era (1600–1868) opium harvests sold to medicine shops provided extra income for peasants in the Osaka region. Opium remained a pharmaceutical, while Japanese—both rich and poor, male and female—enjoyed smoking tobacco from *kiseru* (long-stemmed pipes) and drinking locally brewed sake. Later, when Japan entered the narcotics trade, officials assured each other that the Japanese temperament preferred sake, unlike Chinese people who craved opium. Similar expressions of racial exclusivity marked the general Japanese attitude toward its Asian neighbors as well as their nefarious habit.

In the 1800s, as Western European nations expanded into Asia seeking markets for manufactured goods, Japan remained a closed country, proudly standing aloof from the dangers associated with foreign commerce, trading only with the Dutch at Nagasaki. The Japanese government, under control of the Tokugawa Shogun, denied foreign ships entry to its ports until 1853 when the American Commodore Matthew Perry (1794–1858) backed his entreaty with the threat of force. Within fifteen years new leaders replaced the old samurai regime. Using the authority of the young Meiji emperor (1852–1912), they were determined to create a modern nation with a strong military to guard it.

The closed-country policy of the old order did not mean Japan's governing officials remained unaware of the outside world. They knew that China had fought and lost a war with Great Britain over the opium issue in 1840 and 1842. When Japan finally did open its doors to foreign trade, Article IV of the Treaty of Amity and Commerce of 1858, like those that followed, forbade opium sales. As Japanese trade with Asia expanded, however, Chinese merchants arrived in Japanese ports, bringing their habit with them. In cities such as Osaka or Yokohama, the Chinese enjoyed opium, resulting in periodic police raids on their homes and businesses.

The motivation for opening the nation to foreign trade was the modernization of Japan for protection in a dangerous world. Modernization in the nineteenth century meant expanding the military, producing goods for export, and acquiring colonies. The new Japanese Meiji government excelled in all three areas. In 1894 and 1895 Japan fought and won a war with China, gaining the island of Taiwan off the southern Chinese coast as its first colony. In 1904 and 1905 Japan defeated Russia. As a result, by 1910 Japan owned Korea as a colony and acquired from China the right to build railways and exploit mineral wealth in Manchuria, China's three northeast provinces.

Acquiring Asian colonies forced Japanese government policymakers to reconsider opium. In 1895 the Japanese military prepared to occupy Taiwan, which harbored a Chinese population hostile to the new regime. Taiwan had a substantial population of Chinese opium smokers who acquired their supplies on the open market as the habit was legal in China from 1842 to 1906. As the Japanese Imperial Army faced sporadic warfare against its occupation, the government at home debated extending their opium ban to Taiwan, forcing an already hostile population into opium withdrawal. Many in the government supported a draconian ban on the drug, fearing that opium use in Taiwan would find its way to the home islands.

Gotō Shimpei (1857–1929), a Japanese leader who specialized in public health, offered an alternative. Gotō proposed a colonial monopoly supporting gradual opium withdrawal. His program registered addicts, providing them with legal opium to avoid illicit markets. Complimentary rehabilitation programs weaned addicts away from their habit. Gotō's program granted lucrative opium sales licenses to those Taiwanese who worked with the Japanese government to end anti-Japanese insurrection.

The Taiwan Opium Monopoly system worked well. When combined with parallel monopolies in sugar, camphor, and salt, the colony earned money for the Japanese empire. Addiction rates fell from 169,000 licensed addicts in 1900 to 7,560 in 1941. As Japan's territory expanded—first into Korea, which became a colony in 1910, and then to Manchuria, which became an economic sphere of interest in 1907 and a notorious puppet state under military control in 1932—Gotō's monopoly system followed the spread of empire.

Establishing a functioning government narcotics monopoly created the problem of opium supply. In the beginning Taiwan authorities turned to British Hong Kong for their drugs. In their quest for self-sufficiency, two remarkable men, both with connections to Gotō Shimpei, established careers tied to the monopoly. Nitan'osa Otozō (1875–1950) was a farmer from the Kansai countryside near Osaka. Learning about the opium monopoly, he approached Gotō Shimpei in 1896 with a plan to grow poppies in Japan, releasing the nation from its dependence on British suppliers. With government support, Nitan'osa became an expert on poppies, learning to crossbreed the plant to increase its morphia content. Nitan'osa supplied the Japanese monopoly in Taiwan. As the empire spread to Manchukuo, an elderly Nitan'osa traveled to the puppet state to oversee poppy cultivation in the rich soils of northeast China. He is remembered as Japan's opium king, yet he lived the sedate life of a gentleman farmer.

Hoshi Hajime (1873–1951) specialized in morphine. Hoshi studied business in the United States but returned to Japan where he founded Hoshi Pharmaceuticals in 1910. Japanese morphine came from Germany. Hoshi approached Gotō Shimpei with a plan to manufacture the drug at home from Taiwan opium. As the scheme coincided with World War I, Hoshi's company prospered. Hoshi entered politics and hoped to profit from a stockpiled opium supply he had purchased cheaply from Turkey. His plans failed when political rivals publicly linked his company to a Taiwan bribery scandal. His name suffered further when a British consul determined that the stockpiled opium in Hoshi's bonded warehouses slipped out at night onto the Asian black market.

Hoshi's career exposes a reality that blackened the reputation of the Japanese colonial opium monopolies. On the surface, men who hoped to create a model for addict reform ran the monopolies. Yet the geopolitical climate from the 1910s to the 1930s created temptations and opportunities when China fell into a state of chronic civil war after its 1911 revolution brought an end to the last dynasty. At the same time, Japan's thirty-year expansion into Asia created an empire including

colonies, extensive rail and mining rights in Manchuria, and a commercial presence in major Chinese cities.

In spite of the ensuing chaos, opium became illegal once again in China after 1906, yet the appetite for the drug continued among a significant percentage of the population. Given the unstable situation, the money that could be made satisfying an illicit craving tempted Japanese subjects protected by treaties from Chinese jurisdiction. Korean and Japanese traffickers sold morphine from so-called drug shops in the north. Taiwanese gangsters set up shops along the southern coast, while Japanese soldiers of fortune assisted with both drug trafficking and production. Given opium's illegality, morphine and heroin use increased, especially among China's urban poor. Japanese freebooters specialized in providing a cheaper, high-grade product to this illicit Chinese market.

A business that was lucrative in the 1920s became strategic in the next decade when Japanese militarists created the puppet state of Manchukuo in 1932, and expanded the conflict to an outright war with China in 1937 and into the Pacific in December 1941. In Manchukuo an opium suppression program progressed sporadically, but the number of registered addicts remained static while recovery programs showed high rates of recidivism. Opium from Korea and Manchuria supplied the programs (by 1941 Korea had 8,462 hectares in poppies). Unofficially, narcotics continued to be trafficked into China. The profits went into the secret coffers funding Japanese espionage and such dirty tricks as flooding China with counterfeit currency to ruin the enemy's economy.

CONTEMPORARY USE

The Japanese opium monopoly ended with Japan's surrender to the Allies in August 1945. Records of the bureau, along with eyewitness accounts of illicit activities, entered the files of the International Military Tribunal (1946–1948), adding to the reams of damning evidence against the Japanese military government during the Tokyo war crimes trials.

World War II's end also proved that the sake-loving Japanese would indeed fall victim to drug abuse as addicted soldiers returned home. The most famous addict appears in the novel *Shayo* (The Setting Sun) by Dazai Osamu (Tsushima Shuji, 1909–1948), the bad boy of Japanese literature. Dazai's main character, a drug user, heavy drinker, and womanizer, much like the author, became an icon for dispirited postwar youth.

Japan's connection to morphine ended with its empire, and yet many in the defeated army returned home amphetamine-dependent. During the waning years of the war, the military distributed amphetamines to soldiers and support staff alike. At the war's end the drug proved to be a boon to the home population short on food and desperate to rebuild a war-ravaged homeland. A high level of addiction forced officials to address the effects of easy access to the drug in the 1950s, when a zero tolerance policy reminiscent of the 1868 treaty stipulation became law.

In the economic boom years of the 1980s, however, recreational drug use reappeared. Cocaine, marijuana, and assorted psychedelics all became available, but their use was overshadowed by methamphetamine. Called *shabu* in local slang, meth appeals to the workaholic culture of Japan. Its most vulnerable and loyal cohorts are long-distance truckers working grueling schedules, students cramming for exams, and businessmen (salarymen) also keeping long hours, perhaps remaining awake late into the early morning hours over a game of mahjong or poker. Adolescents who abuse solvents often turn to methamphetamine later in their lives. Japanese organized crime (*yakuza*) supplies the illicit market, obtaining its drugs from Thailand, China, Myanmar (the former Burma), or Taiwan. The official approach to addiction is the imprisonment or institutionalization of addicts. One nongovernmental group, the Maryknoll Alcoholic Center/Drug Addiction Recovery Center, treats addiction through self-help. Created by two former addicts who began to hold meetings in places where addicts gather, the organization had grown to 70 facilities by 2006.

Alcohol and tobacco remain the primary addictions in Japan. Japan has a long tradition of brewing sake and distilling *shochu*. The opening of its doors to the West added beer to the national offering. It was only after World War II that a wide range of foreign alcohol became available and popular. Drinking in Japan is a social activity, especially for the workforce for whom after-hours socializing in bars is sometimes typical. Strict traffic laws, an available and extensive public transit system, and

the social tolerance of late-night drunks, sometimes intoxicated drinkers help to reduce the fatalities often associated with after-hours drinking. The social nature of drinking, however, means that as the population demographics age, the percentage of drinkers is declining. In the same way, during periods of national stress, such as the Hanshin Earthquake of 1995, alcohol consumption unexpectedly decreased.

Tobacco use began in the 1600s and quickly spread throughout Japanese society, in spite of early government bans. Ornate, small-bowled pipes with long stems adorn woodblock portraits of famous actors and geisha of the Tokugawa period. After Japan was opened to foreign trade, new types of tobacco and methods of smoking were introduced. By 1904 the Japanese government taxed and controlled tobacco products. During the postwar period tobacco products produced via the government monopoly dominated the home market as high tariff barriers made foreign cigarettes a luxury. Under foreign pressure, tariffs eased in 1986, at which time advertising increased the popularity of smoking. Once a government monopoly, in 2000 the Japanese Ministry of Finance owned 67 percent of Japan Tobacco Inc., which controls cigarette production and distribution throughout the nation.

Public awareness of the health risks of cigarettes lowered the number of smokers throughout the 1990s. Once rare, smoke-free areas are sporadically available in the early twenty-first century. Evidence of such changing attitudes may be observed in the glowing cigarettes of the firefly tribe (*hotaru zoku*), those smokers whose wives or colleagues force them to smoke outside. Nevertheless, with male smokers estimated at 52.8 percent in 1999, Japan still has the largest smoking population in the developed world. And, the percentage of female smokers is on the rise. The sale of alcohol and tobacco to youth under the age of 20 is legally banned, but the law has little tangible effect in a nation where open-air vending machines offering both commodities may be found everywhere.

ASSESSMENT

Japan's history of monopoly regulation of addictive substances is bipolar at best. The colonial experience with narcotics demonstrates that an addict population may be reduced as the result of implementing such a system, as was the case in Taiwan, but the potential for easy and large profits can create dangerous failures within it. In the twenty-first century the Japanese government's continued involvement in the tobacco industry hampers the aggressive kind of anti-tobacco campaign that has proven so effective in other developed nations.

See also **Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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JARGON. *See* **Slang Terms in U.S. Drug Cultures.**

JELLINEK MEMORIAL FUND. In 1955 the Jellinek Memorial Fund was established to commemorate E. M. Jellinek (1890–1963) and his great contribution to the field of alcohol

studies. A capital fund was developed, and the interest from this fund has been used to provide an annual cash award to a scientist who has made an outstanding contribution to the advancement of knowledge in the alcohol/alcoholism field. The first award was presented in 1968.

Each year the board of directors of the Jellinek Memorial Fund designates the specific area of research for which the award will be made and appoints an Expert Selection Committee to review candidates and recommend an appropriate awardee. The awardee may be selected from any country, the sole criterion being the scientific contribution that the person has made within the selected category. The award is traditionally presented at a major international conference, and, if necessary, travel and accommodation expenses are provided to permit the winner to attend the conference for the presentation.

The following general criteria have been accepted by the board and by previous selection committees as guidelines:

1. The award is to be given to the person deemed to have made, during the preceding years, the greatest scholarly contribution to human knowledge of problems relating to alcohol, in the designated research area.
2. The person selected for the award should be someone who would provide an example and serve as a model for others who might be attracted to work in the field.
3. Only living scientists should be considered for the award.
4. Advanced age or impending retirement would not disqualify someone from candidacy. However, if two or more scientists were considered approximately equal, the one more likely to continue longer in the field would be favored.
5. If the outstanding contribution of a candidate was made more than ten years earlier, consideration for the award would require evidence of the candidate's continuing interest and active participation in alcohol research.
6. Other factors being equal, the person would be favored whose primary identification continued to be in the field.
7. If a member of the Expert Selection Committee is deemed eligible for the Jellinek Award, the chair of the selection committee should consult with the president and request the resignation of the committee member.
8. If a previous award winner becomes a candidate and appears equal to or above all other candidates on the basis of unique new achievements, he or she should not be ruled ineligible. The chair of the selection committee should consult with the president to ensure that the award is for new achievement and determine if he or she is eligible.
9. The award will normally be made to an individual researcher most highly recommended by the selection committee. In special circumstances, if the selection committee recommends two persons of equal and outstanding merit, a joint award may be made to the two.

In 2007, the award was given in the category of epidemiology and population studies to Bridget F. Grant, Ph.D., Chief, Laboratory of Epidemiology and Biometry, Division of Intramural Clinical and Biological Research, at the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health. Grant received the award for demonstrating leadership in the design, implementation, and analysis of major epidemiologic surveys focused on alcohol and drug use disorders and their relationship to other psychiatric disorders. Other winners have worked in the areas of biological and medical research (2004); social, cultural, and population studies (2005); and behavioral studies (2006).

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JEWS AND ALCOHOL. Compared with other religious and ethnic groups, Jewish Americans have an unusual pattern of involvement with alcohol. Studies in the United States consistently

find that across religious groups, Jews report the lowest rate of abstinence, with only 6–13 percent being lifetime abstainers (Beigel & Ghertner, 1977; Calahan, 1978; Cochran et al., 1988). Even so, Jews have lower rates of alcohol use disorders. Lifetime rates of alcohol abuse and dependence are approximately 11 percent for Jewish males, compared to 29 percent for non-Jewish males, and 3 percent for Jewish females, compared to 9 percent for non-Jewish females (Levav et al., 1997). Research in the United States and in Israel has found that Jews are less likely to engage in heavy drinking episodes (also known as binge drinking), compared with non-Jews (Luczak et al., 2002; Monteiro & Schuckit, 1989; Neumark et al., 2003).

The etiologic basis is unclear, but researchers hypothesize that these differences result from both psychosocial and biological factors. Early theories concentrated on religious and cultural explanations for the lower levels of alcohol use disorders among Jews; more recent studies have focused on possible biological and genetic influences.

INFLUENCE OF RELIGION

Early theories on the low rates of alcohol use disorders among Jews focused on the symbolic importance of alcohol in the religious (Orthodox) Jewish community. Through the study of Judaism and participation in religious ceremonies, Robert Bales conducted research (1946) that suggested that Jews learn to drink in moderation, and use alcohol primarily for ritualistic purposes. Building on Bales's theory of ritualized drinking, Charles Snyder (1958) hypothesized that as Jews integrated into greater society and became less religious (moved away from or left Orthodoxy), heavy drinking and related problems would increase. To test his ingroup-outgroup theory, Snyder studied nominal religious affiliation and lifetime rates of drinking to intoxication in male Jewish college students and adults. He found the rate of reported intoxication significantly increased with decreased Orthodoxy. Additional support for Snyder's hypothesis comes from a survey of Jewish adults living in Israel. A higher proportion of Orthodox Jews reported being current drinkers, but they drank less frequently and more often for ritualistic purposes than secular Jews (Kandel & Sudit, 1982).

Methodological and interpretive concerns have been raised in reference to these early studies (see Flasher & Maisto, 1984, for a review), and some reports have not found significant relationships between Jewish denomination and drinking variables (Bar-Lev, 1985; Kumpfer & Room, 1967). However, more recent research on college students and general samples continues to support the notion that individuals from more religious denominations report lower rates of intoxication and heavy drinking compared with those from less religious denominations and those who are not Jewish (Hasin et al., 1999; Luczak et al., 2002; Neumark et al., 2001).

Specific religious variables also have been tested in relation to alcohol involvement behaviors. In Jewish American college students, low strength of religious commitment has been linked to heavy alcohol use and negative consequences (Perkins, 1985). In Israel, adherence to Jewish religious requirements was inversely related to frequency of drinking and drunkenness (Aharonovich et al., 2001; Hasin et al., 1999; Rahav et al., 1999). However, religious service attendance did not relate to binge drinking in Jewish American college students (Luczak et al., 2002), nor has it been associated with alcohol use and perceived misuse in Jewish American adults (Cochran et al., 1988). It is possible that some measures (such as service attendance) have more or less salience across religions and thus relate to alcohol variables differently across groups.

INFLUENCE OF CULTURE

It has been hypothesized that Jews are not just a religious group; they are also an ethnic minority with a set of cultural values. Common practices such as eating traditional foods, feeling connected to Israel, engaging in certain customs, singing Jewish songs, and feeling a bond to the Jewish community can be considered components of "Jewish" culture (Langman, 1995). This affiliation also may include religious practices, but it focuses primarily on the solidarity and norms set out by the group. As early as 1947, Donald Glad attempted to summarize this "cultural" view of Jews in relation to alcohol involvement. Although he agreed with Bales (1946) that moderate alcohol use may be learned in the Jewish community through conformity to certain religious customs, he also asserted that other factors, such as group norms,

may have a more global influence on alcohol use. He cited factors such as family permissiveness and the strong Jewish sanction against drunkenness as being learned through the affiliation with the group as a whole. He argued that the stigmatization of public inebriety among Jews is captured by the Yiddish expression, "Shikker iz a Goy" (The drunkard is a non-Jew).

In his study of Jewish, Irish, and Protestant male adolescents, Glad (1947) found Jewish adolescents had fewer feelings of guilt regarding drinking, had a younger mean age when they felt permitted to drink, and were more likely to report drinking with their parents. More recent research also has supported the distinction between religious and cultural influences. In a study of drinking patterns among different religious groups in the United States, Freund (1985) found that a liberal family attitude toward moderate drinking was associated with low rates of inebriety regardless of the ritual (religious) reinforcement of sobriety. Greater Jewish cultural identity also has been related to moderate alcohol consumption in young adults (Bar-Lev, 1985), but cultural identity was not associated with binge drinking in college students (Luczak et al., 2002). Taken together, these studies suggest that being a member of the Jewish community and identifying with Jewish culture may protect against heavy alcohol involvement separate from the religious aspects of Judaism.

INFLUENCE OF BIOLOGY AND GENETICS

Along with psychosocial theories, biological explanations have been hypothesized to explain the low level of alcohol problems in Jews. Most self-identified Jews in the United States originate from common eastern European backgrounds (i.e., Ashkenazic Jews) and tend to marry within their religion. Thus, the group is relatively homogeneous and may possess genetic traits that could influence risk for various disorders. In support of this hypothesis, Jews have a significantly lower rate of family history of alcoholism (Monteiro & Schuckit, 1989), one of the strongest and most consistent risk factors for this disorder. The increased risk for alcohol use disorders in people with a family history of alcoholism is mediated by both biological and environmental factors. One important biological factor associated with both family history of alcoholism and vulnerability to alcohol use disorders is an individual's sensitivity to alcohol (Schuckit, 2000). A low level of response to alcohol has been related to increased risk, and a heightened response has been associated with relative protection from alcohol dependence. In support of a biological theory for the lower rates of alcohol use disorders in Jews, Jewish American male college students were shown to experience more intense reactions to a moderate dose of alcohol than non-Jewish American male college students (Monteiro et al., 1991).

Polymorphisms in several genes encoding isoenzymes involved in alcohol metabolism have been associated with enhanced sensitivity to alcohol and protection against alcohol use disorders (Li, 2000). One such polymorphism of the alcohol dehydrogenase gene *ADH1B*2* has been found in higher prevalence in Jews (32–49%) compared with non-Jewish Caucasians (2–8%). The highest rates of the *ADH1B*2* allele are found in northeast Asians (90–92%), another group with relatively lower rates of alcohol use disorders (Goedde et al., 1992; Neumark et al., 1998; Shea et al., 2001).

Possession of *ADH1B*2* in relation to a variety of drinking variables has been studied in Jews. Jewish men with *ADH1B*2* report more unpleasant alcohol symptoms, such as flushing, nausea, and headaches, compared with men without the allele (Carr et al., 2002). *ADH1B*2* has also been associated with less frequent drinking (including heavy drinking) in college and adult samples of Jewish Americans and in Israeli general and treatment samples (Carr et al., 2002; Hasin et al., 2002a; Luczak et al., 2002; Neumark et al., 1998; Shea et al., 2001; Spivak et al., 2007). Finally, *ADH1B*2* has been related to lower lifetime alcohol dependence severity in a community sample of Israelis (Hasin et al., 2002b). Taken together, these findings suggest the *ADH1B*2* allele has a protective effect on a range of alcohol involvement variables in Jews.

The extant research suggests religious, cultural, and biological factors all contribute to explaining the unusual pattern of alcohol involvement found in Jews. Their relatively low rates of abstinence and alcohol use disorders are likely due to a confluence of factors. How these factors combine and interact should continue to be explored in prospective studies that incorporate biopsychosocial models. Such research will provide important insights into the

relationship between Jews and alcohol. However, the research should be tested for generalizability to enable better understanding of the mechanisms by which some individuals might be protected from developing alcohol problems.

See also **Risk Factors for Substance Use, Abuse, and Dependence: Race/Ethnicity; Religion and Drug Use.**

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JIMSONWEED. Jimsonweed is a tall, coarse, poisonous plant that flowers, produces seed, and dies in one year. It belongs to the nightshade family (Solanaceae), and has foul-smelling leaves and large white or violet trumpet-shaped flowers. It produces round, prickly fruits. Jimsonweed (*Datura stramonium*) grows in several parts of the world. A strong intoxicant made from this plant was used by the woodland tribes of eastern North America. The plant was also used as an ingredient of wysoccan, an intoxicant employed in the puberty rites of Native Americans in what is now Virginia. Indeed, the name Jimson is another form of Jamestown, the English colony founded in Virginia in 1607.

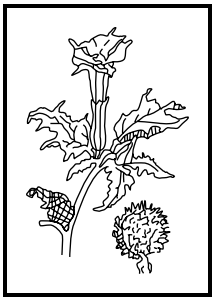

Figure 1. Jimsonweed. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Smoke from burning jimsonweed was inhaled to relieve symptoms of asthma in India, and cigarettes containing jimsonweed have also been used for the same purpose.

As in other members of the Solanaceae family, the mind-altering substances are tropane alkaloids, and the seeds and leaves contain up to 0.4 percent of these compounds. The principal alkaloid found in jimsonweed (also found in belladonna) is atropine. Atropine widens the pupils of the eyes, helps stop muscular spasms, lessens pain, and reduces bodily secretions. Large to toxic doses of atropine result in restlessness, irritability, disorientation, hallucinations, and delirium.

See also **Plants, Drugs From.**

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ROBERT ZACZEK
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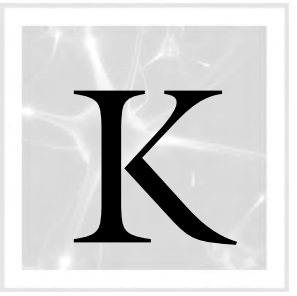

KAVA. Kava is a drink prepared from the root of the Australasian pepper shrub *Piper methysticum*. The word *kava*, which is Polynesian for bitter, pungent, is given to the drink because of its strong peppery taste. Several variations of this drink were once used widely as social intoxicants in the islands of the South Pacific, particularly Fiji. The quality of the drink improves with the age of the root, and the roots are generally at least four years old before they are used. After the root is cut and crushed or grated, the active components are extracted by soaking the preparation in water.

Common effects of kava include general muscular relaxation, euphoria, and loss of fatigue. Visual and auditory effects are also common. In large quantities kava can induce muscular incoordination and ultimately stupor.

While no alkaloids or glycosides have been found in kava, several aromatically substituted α-pyrones, including kawain, dihydrokawain, methysticin, and yangonin, have been isolated from the extracted root. Other as-yet-unidentified components of kava may also be important in the effects of the drink.

See also **Plants, Drugs From.**

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ROBERT ZACZEK

KENYA. Psychoactive substances in Kenya are a source of concern both nationally, due to a perceived rise in consumption levels, and internationally, as Kenya has become a significant entrepôt, or distribution center, in global trafficking networks (International Narcotics Control Board, 2007). Kenyan psychoactive substances include fermented beverages, khat (known as *miraa* in Kenya), cannabis, and tobacco (whose usage can be traced back centuries), as well as distilled spirits, heroin, cocaine, solvents, and Mandrax (methaqualone), introduced much more recently. These substances are considered in this essay; tea and coffee—while stimulants and of great economic importance to the country—are beyond the present entry's scope.

ALCOHOLIC DRINKS

By far the most commonly consumed substances in Kenya are alcoholic drinks—brews made from grains, fruits, and honey are as widely consumed as ever, especially in rural regions. Age-old drinks include those brewed from millet, sorghum, honey, and sugarcane as well as palm wine (made from fermented palm sap), a popular beverage on the coast. Idealized accounts of traditional consumption report that such drinks were restricted to male elders who would gather round the communal beer pot each with their own straw. Such accounts of past drinking as socially integrative are compared with a perceived lack of control in present day drinking practices (Willis, 2002).

During much of the colonial era, bottled beer and spirits were legally restricted to Europeans. Such restrictions lasted until 1947, after which consumption of bottled beer by the African population grew massively, along with the East African brewery industry. While traditional brews became the drink of the rural areas, bottled beers were associated with urban sophistication and modernity. Post-independence, advertisers even marketed bottled beer as the drink of a successful nation. Opposition and ambivalence to all types of alcohol exists in the early twenty-first century, but the greatest concern is for *chang'aa*, an illicitly distilled spirit available cheaply in most towns and villages. This drink, distilled using homemade equipment, is reportedly often adulterated with pure ethanol to strengthen the already heady liquor.

KHAT

Khat consists of the stimulant stems and leaves of *Catha edulis*, a tree indigenous to forests throughout Kenya but is also cultivated in several areas, the most important being the Nyambene Hills district northeast of Mount Kenya (Carrier, 2007). This mountain range is home to the Meru, whose economy is greatly dependent upon khat. Explorers in the late nineteenth century reported the keen chewing of khat by Meru elders (Neumann, 1898), and by that time the crop was already cultivated and exchanged. The growth of nearby Isiolo, with its khat-chewing Somali residents, spurred on farming and trade and, by the mid-twentieth century, khat was sold as far afield as Nairobi and the coast, despite attempts by the British to restrict it.

Khat is incorporated into many local ceremonies—for example, in the Nyambenes a specially packaged bundle of khat is used in brideprice negotiations—and is now intertwined with Meru and Somali identity. Its consumption is also associated with coastal Swahili, Muslims more generally, and has been absorbed into a pan-ethnic youth culture. Much khat chewing takes place in leisure contexts, but its stimulating properties—its main active constituent, *cathinone*, has the effect of a mild amphetamine—are also used by nightwatchmen, drivers, and students in work contexts (Zaghloul, Abdalla, El Gammal, & Moselhy, 2003). Consumption is linked to insomnia, and sedatives such as *rohypnol* and *piriton* are used by some to counter its effects; others claim drinking milk or beer is effective in inducing sleep.

Khat is exported, much of it being flown to Somalia, Europe, or North America for consumers among the Somali diaspora. This international trade flourishes despite its illegal status in many countries. There is vigorous debate in Kenya as to the social and health impacts of the substance and if it should be banned. However, such is its economic importance for farmers and traders throughout the country as well as its value as a foreign exchange earner that it seems immune to legal restriction.

TOBACCO

While not indigenous to East Africa, tobacco smoking, chewing, and sniffing had already penetrated the interior of the region long before British rule was established, most likely brought by Spanish and Portuguese sailors in the late sixteenth or early seventeenth centuries. Certainly by the late nineteenth century, explorers, such as Neumann (1898), were often offered tobacco by groups encountered far from the coast. The crop became highly commercialized during the twentieth century, and today smallholders in several regions of the country supply British American tobacco with sufficient quantities to satisfy the Kenyan demand for cigarettes, and for export. Growing tobacco has been profitable for some farmers (see Heald, 1991 and 1999 on tobacco farmers in Kuria district), but there is much ambivalence about the crop and its consumption. Antismoking campaigns have begun in earnest, and in 2007 Parliament passed a Tobacco Control Act regulating manufacture and sale. It is also raising awareness of tobacco's dangers through explicit health warnings on packets. In addition, in Nairobi, Mombasa, and Nakuru local bylaws now restrict smoking in public places. Evidence shows that annual per capita cigarette consumption has fallen since the late 1980s, although prevalence is still high according to an online report by the World Health Organization (2003). As antismoking campaigns intensify, there are concerns that falling sales might affect thousands of farmers reliant on tobacco unless they receive support to grow alternative crops.

CANNABIS

Cannabis in East Africa has not yet been studied as thoroughly as alcohol or khat, but even so it has a long history in the area. Cannabis is called *bangi* and may have been introduced through centuries-

old Indian Ocean trade links. Like khat, cannabis is consumed both in leisure and work contexts; people believe it is useful when working at arduous physical tasks. Unlike khat, cannabis is illegal; possession and supply are subject to prison terms and hefty fines, so cultivation is hidden. Often the crop is grown among sugarcane in Western Kenya or deep within the forests on Mount Kenya. Indeed, there is concern at the destruction of forest to make way for cannabis. The coast also has a significant number of plantations. Cannabis is inexpensive in Kenya and has become a commercially significant crop with a large local market. Profit can be made on the coast where there is much demand for cannabis from Western tourists. Regarding exports, the United Nations Office of Drug Control and Crime Prevention (UNODCCP) reported in 1999 that up to 50 percent of Kenyan-produced cannabis is exported to neighboring countries and Europe.

HEROIN

Heroin use in Kenya first became apparent in the 1980s, especially in Nairobi and on the coast (Beckerleg, Telfer, & Sadiq, 2006). Some connect its spread to tourism, especially in towns such as Malindi, where a tourist boom in the 1980s increased the number of European visitors requesting the drug and brought locals into contact with it. Originally heroin was consumed by inhaling the vapor of "brown sugar," but in the late 1990s "white crest" appeared on the market, a variety from Thailand that is injected. Thus injecting became more common, a practice especially dangerous given the prevalence of HIV. A 2005 survey of 336 heroin users in Nairobi found "that 44.9% were, or had been, injectors" and that over half the current injectors were HIV positive (Beckerleg, Telfer, & Hundt, 2005, p. 1).

The growth of heroin use on the coast has been alarming and has spurred the creation of the Omari project in Watamu to provide support for those wishing to give up heroin. Much outside attention has focused on Kenya and heroin not because of consumption within the country, but more for its role as an entrepôt in transnational trafficking networks. Traffickers taking Southeast- and Southwest-Asian heroin to Europe have targeted the Mombasa port and the Nairobi international airport as relatively safe nodes in such networks. There have been some attempts to cultivate opium poppies in Kenya, and in October 1989 police destroyed a plantation of 30,000 plants (United Nations Office of Drug Control and Crime Prevention, 1999, p. 21).

OTHER SUBSTANCES

As with heroin, Kenya serves as an entrepôt for cocaine and methaqualone (Mandrax), a sedative popular in South Africa. There are reports that cocaine is used by wealthy students in large Kenyan towns and that Mandrax is also used by Kenyan students; however, these two substances seem to pass through Kenya en route to Europe, in the case of cocaine (smuggled initially from South America), and to South Africa, in the case of Mandrax (smuggled initially from India). Some laboratories have started producing the substance in Kenya for sale in South Africa. One such factory was discovered in 2007, according to a report by the Kenya Broadcasting Corporation.

Of great concern is the inhalation of solvents by street children, and the sight of young children clutching plastic bottles containing glue is tragically common in urban areas. Of less concern is the consumption of betel leaf/areca nut. This chewable combination has been produced on the coast for centuries and, although still mostly consumed by Asians and Arabs, its use has spread to the African population—it is sold in large towns throughout the country. It is often consumed in combination with tobacco paste, so betel/areca nut use is linked to oral cancer (Warnakulasiriya, Trivedy, & Peters, 2002). Small sachets of Indian-produced *gutka* (containing areca nut, chewing tobacco, and flavoring) are also available. In 1999 UNODCCP reported amphetamine usage in Kenya, although it is hard to gauge the scale of its trade and use.

DRUGS REGULATIONS, POLICIES, AND FEARS

The legal status of the above substances in Kenya varies. Khat is available without restrictions, while alcohol in the form of *chang'aa* is illegal, although its trade still flourishes. Cannabis, heroin, cocaine, and Mandrax are illegal and subject to severe penalties introduced by the Narcotic Drugs and Psychotic Substances (Control) Act of 1994. There is an Anti-Narcotics Unit within the police force to enforce current legislation. Cannabis-related arrests are by far the most prosecuted offenses, and often

number around 4,000 annually (UNODCCP, 1999, p. 98). The media have reported a number of highly publicized seizures of heroin and cocaine since the late 1990s, but high levels of corruption are frustrating the fight against trafficking (Mgendi, 1998).

The 1994 act also provided for the establishment of treatment and rehabilitation centers. While nongovernmental organizations run such programs as the Omari Project on the coast, the Kenyan government itself has established a drug rehabilitation unit in Mathari Hospital, Nairobi. Also, a parastatal organization called *The National Campaign Against Drug Abuse* (NACADA) leads educational initiatives in schools and universities and voices concerns over drug use through the Kenyan media. The greatest worry is a rise in consumption by Kenyan youth, and a 2003 NACADA report is titled "Youth in Peril."

The notion that youth are especially at risk from substance use is not new in Kenya and reflects the concern that younger generations are badly affected by rises in poverty, unemployment, HIV, and other pressing factors: The UNODCCP report of 1999 links drug use by Kenyan youth to these socioeconomic factors. Many health workers, religious leaders, teachers, and community leaders express strong fears that drug use will continue to worsen (UNODCCP 1999, p. 35). However, much commentary on substance use in Kenya is perforce rather impressionistic given that scant research—quantitative or qualitative—has been conducted so far. It is hoped that future research will elucidate the situation further and assist in developing policies and treatment facilities sensitive to Kenya's needs.

See also **Africa; Foreign Policy and Drugs, United States; International Drug Supply Systems; Nigeria; South Africa.**

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NEIL CARRIER

KHAT. *Catha edulis*, commonly known as khat, qat, chat, or miraa, is a tree or shrub that grows wild across highland areas of much of Africa and Western Asia, at altitudes of between 5,000 and 6,500 feet above sea level. Wild khat trees can grow as high as eighty feet in an equatorial climate, although the farmed variety is kept at around twenty feet with constant pruning. Cultivation and use of khat go back for centuries, and its use is deeply embedded in the cultures of Yemen, Ethiopia, and parts of Kenya.

The harvested commodity varies from region to region as to what is considered edible and how it is presented. Either the leaves or tender stems from the khat shrub are worked into a wad in the cheek

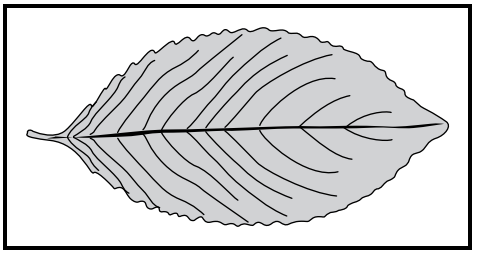

Figure 1. Khat leaf. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

of the consumer. These are masticated over the course of the khat session, lasting between two and eight hours depending on context and occasion. To neutralize the bitter taste of khat, sweet drinks are imbibed, traditionally tea, but increasingly carbonated drinks. In most settings in Ethiopia, Somalia, and Kenya, khat chewing has become associated with nicotine consumption either with cigarettes or by using hubbly bubblies (a colloquial name for hookah).

The legal status of khat varies around the world and is subject to review and revision by the governments often acting on the advice of the World Health Organization and the UN Office on Drugs and Crime. Khat is a legal substance in Yemen, Ethiopia, Djibouti, Kenya, and Uganda, but it is illegal in Tanzania and Rwanda. It is imported into Somalia daily but has been blamed for fueling the war and chaos that bedevils that country. It is legal in the U.K. and the Netherlands but is an illicit substance in the United States and Canada.

HISTORY

The first known reference to khat in Ethiopia is in the fourteenth-century chronicle of the Ethiopian emperor Amde Zion, in which the Sultan of Ifat is quoted as saying: "I will take up my residence at Mar'ade, the capital of his [Amde Zion's] kingdom and I will plant chat [khat] there because the Muslims love the plant" (Gebissa, 2004). Since about 1400 CE in the city of Harar, the capital of the Hararge region of Ethiopia, Islamic leaders have consumed khat leaves to stay awake during Ramadan. Merchants used it to facilitate long-distance travel, and farmers chewed it regularly throughout the day. Production and consumption were originally limited to Muslims, but over the centuries khat gained an important place in rituals of piety in Islamic observance, particularly in the Hararge region. For centuries it has been a standard practice for those who participated in religious ceremonies held at the Muslim shrines to spend long hours of the day and night chewing khat while reciting passages from the Holy Qur'an and praying. In Ethiopia some devout Muslims even consider khat holy, refer to it as the flower of paradise, and often offer prayers before they begin to chew it. Although the origins of khat consumption are sometimes linked to the need for Islamic scholars in the Hararge region of Ethiopia to stay awake, the use of khat by Muslims is a source of controversy.

Linguistic evidence points to Yemen as the earliest region to use *Catha edulis* (Ethiopian *chat* is derived from Yemeni *qat*), although Ethiopian documents record dates for khat being sent from Harar between the thirteenth and fifteenth centuries, and the Yemeni records indicate a later introduction. Khat is mentioned by al-Miswari of Ta'izz in the thirteenth century, but he may have been referring to a tea made from khat leaves. Khat is absent from a plant register drawn up for the king of Yemen in about 1271, and Ibn Ibn Battuta, the great traveler, failed to spot it in 1330. It is most likely that khat was introduced to Yemen by Sufi travelers in the late fourteenth century or the early fifteenth century. By the sixteenth century khat was well established in Yemeni religious and legal texts. The theological debate dates from the fifteenth and sixteenth centuries, when arguments focused on the degree to which the plant could be considered an intoxicant and should be placed in the category of *haram* (forbidden) substances, along with alcohol and hashish. Some scholars argued that analogous to wine, khat has consciousness-altering properties, and because it is on the basis of such properties that alcohol was forbidden by the prophet, khat too should be forbidden. However, the prevailing legal ruling in Yemen in modern times has been the more literal Islamic interpretation, that because it was not explicitly mentioned in the Qur'an it should not be forbidden.

Khat, more often known as miraa in Kenya, has been used for centuries in part of the Nyambene Hills within the Meru district. Khat from particularly old trees has long been used by the Meru clans of Igembe and Tigania for ceremonial presentation in brideprice negotiations, requests to elders for

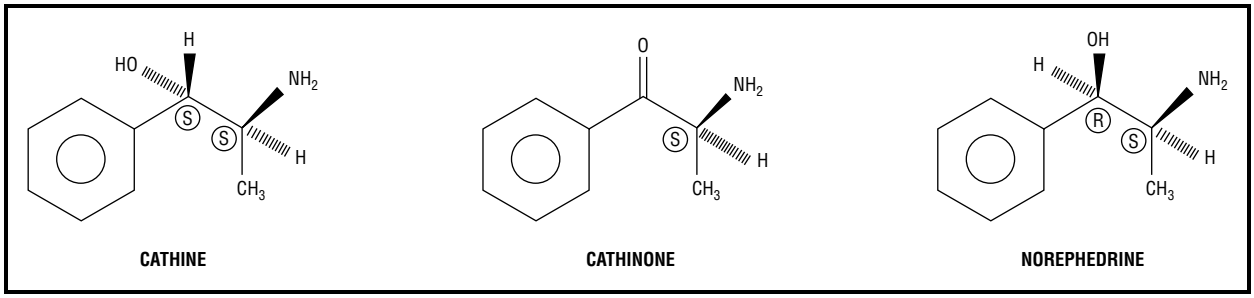

Figure 2. Structure of khatamines. Cathine (S,S(+)phenylpropanolamine or (+)norpseudoephedrine), cathinone (S(−)alphaaminopropiophenone) and norephedrine (R,S(−)phenylpropanolamine). In an analysis of twenty-two khat samples of different origin, the average concentration of these alkaloids in 100 grams of fresh khat were found to be 120 milligrams, 36 milligrams, and 8 milligrams, respectively. (Geisshüsler & Brenneisen, 1987). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

circumcision to proceed, and in peacemaking. Farmers also chew a few stems as they work, but most still do not indulge in heavy khat consumption. Most substance-related problems are only indirectly related to khat, in that the farmers and merchants profiting from this lucrative export often convert a good part of their earnings into excessive alcohol consumption.

A mixed agricultural system that now has khat as its main cash crop was developed by the Igembe and Tigania clans who, from the nineteenth century, marketed and distributed khat to an ever widening market, first within Kenya and then beyond. From the mid-twentieth century, Yemeni and Somali Kenya citizens scattered throughout the country provided a ready market for khat from the Nyambene Hills. As consumption spread to different districts and ethnic groups, a khat subculture and associated language to describe khat and its effects developed. Khat has come to dominate daily life among many Somalis living in cities, rural areas, and refugee camps. As chewing spread, local names for khat such as murungi, veve, and gomba emerged. At the coast Yemenis introduced miraa-chewing to the Swahili whom they lived among and intermarried with. Yet, as khat consumption spreads, controversy about its use continues to grow. Many Kenyan government and civil society organizations consider khat to be a harmful substance and claim that it exacerbated the civil war of the 1990s in Somalia and impedes development in the ethnic-Somali dominated area of North Eastern Province.

PHARMACOLOGY

Khat has been known in the West for over two hundred years after samples of the plant were collected in Yemen by the Swedish botanist, Pehr Forsskal (1732–1763). Forsskal identified and classified khat as *Catha edulis* and made the first detailed botanical description of this evergreen shrub of the Celastraceae family.

The pharmacological study of the properties of *Catha edulis* dates back to 1887 when the alkaloid cathine, or d-norpseudoephedrine, was identified as the first active ingredient. The main active ingredient, cathinone, was not isolated until the 1970s. In fresh leaves cathinone combines with a second alkaloid of cathine, norpseudoephedrine, and several other alkaloids, tannins, and other ingredients. Cathinone is highly volatile and breaks down rapidly in leaves and stems once twigs are cut from the live plant.

The constituent mainly responsible for the stimulant qualities and the dependence-producing effects of khat is cathinone. This alkaloid must be considered a natural amphetamine, as the two substances have the same mechanism of action. However, cathinone has a half-life of only one and a half hours, whereas amphetamine is much longer. Because cathinone is absorbed gradually from the leaves during chewing and is inactivated in the body rather rapidly, the pharmacological effects of khat are usually limited.

EFFECTS

Khat stimulates the central nervous system, resulting in a state of mild euphoria and excitement, often accompanied by talkativeness. Chewers report an immediate emotional effect of euphoria, which increases the sense of well-being and can

facilitate social interaction. This initial euphoria is followed by a quieter, more introspective mood. This is the phase celebrated in Arabic poetry, and the period when musicians receive their inspiration. Contemplation often turns melancholy. It is at this point that a communal khat-chewing session usually breaks up as the chewers disperse. Experienced chewers know that the melancholic phase is typical and are able to adjust their mood so that negative thoughts and feelings are minimized or eliminated. Some chronic users have been found to carry on chewing in order to postpone the comedown. There are suggestions that the effect of khat is largely conditioned by the context, the company, and the expectations of the user, known among drug researchers as the *set* and *setting*.

Chewing khat tends to cause insomnia. Sleeplessness is sometimes the desired effect, for example, in Ethiopia for staying awake and reading the Qur'an. Across East Africa it is used as a concentration aid by university students, truck drivers, and night watchmen. Africans chew to remain alert; in Uganda night-clubbers use khat to help them dance all night. Those khat consumers who want to sleep may resort to other substances to counter the stimulant properties of khat. Hence, many consumers in Uganda choose alcohol after chewing, whereas many Somalis resort to Valium, which is cheap and easily available on the black market in many East African countries.

Like all stimulants, khat disrupts sleep patterns and proves exhausting after repeated use. The disturbances of natural bodily, as well as social, rhythms can cause disturbances in the mental well-being and social adjustment of some users. For most users, the recovery phase is fairly benign, particularly when compared to that of other drugs. Individual chewers learn to identify the specific effects khat has on them, and they regulate their use to achieve the desired effects. Nevertheless, the pleasurable effects of chewing appear to be broadly similar among chewers regardless of location or culture. Hence, the term *kayf* expresses the experience of the khat-high in Yemen, while in Kenya, Somalia, and Uganda the term *handas* with the same meaning is widely used to describe similar effects. These pleasurable effects are not generally considered by researchers to lead to physical dependence, although there is some evidence of the problems typically associated with drug addiction; for example, general malaise, trembling, and bad dreams appear to be physiological responses to drug deprivation. These symptoms suggest that a mild form of physiological dependence does result from extremely heavy use.

Nevertheless, most khat users can come off the substance and find relief from unpleasant side effects after short periods of abstinence. In Yemen, Ethiopia, and parts of Kenya, traditional cultures of consumption have set parameters for safe and moderate use. These checks on harmful consumption patterns are absent in settings in which new consumers have taken up recreational chewing and often mix khat with alcohol or cannabis. In areas in which khat use is newer, for example, in East Africa or in the wider Somali diaspora, rituals and customs associated with chewing have not as of 2008 been elaborated and established. The pattern of khat use in most parts of Kenya and Uganda is similar to that in the U.K., in that it is an entirely secular form of recreation with no root in local culture. Language and ceremony are borrowed from older cultures of use and evoke, in the case of Somalis, a tradition that is in fact very recent. There is no religious or ritual dimension to use, and the khat chewing session is not integrated into social life but a semi-clandestine addition to it. It is possible that without such culturally embedded controls on consumption as were developed in Yemen and Ethiopia centuries ago, excessive use might trigger a range of psychiatric conditions.

Chronic khat use can lead to high levels of intoxication that may trigger disorders. These include observed loss of appetite, mood swings, anxiety, insomnia, irritability, and depression. Links between khat use and paranoid psychosis and hypomanic illness with grandiose delusions have been reported from case studies in the United Kingdom as well as Somalia and Kenya. International research on the implications of khat use for mental health was ongoing as of 2008. Studies abound linking khat use with a range of adverse conditions, yet none has been based on sufficiently large sample populations or has been able to discount confounding factors, such as post-traumatic shock and cultural dislocation among Somali refugees, to allow for firm conclusions to be drawn either way. Many psychiatrists and mental health

Khat is said to produce a feeling of euphoria when chewed. AP IMAGES.

practitioners working in the field agree, however, that khat is a powerful trigger for a range of conditions. What remains to be determined are dosage, usage patterns, contributing factors, and individual predisposition.

The most harmful effects of khat chewing are related to the budgets of poor people who cannot afford to buy the substance as well as care properly for their families. The point that khat use is detrimental to family life and finances is emphasized by Somali groups living in the diaspora. In addition, detractors of khat attribute its use to increases in idleness, a decline in morals, female prostitution, criminality among male youth, and the erosion of the family.

KHAT USE IN EUROPE AND NORTH AMERICA

One striking aspect of the khat industry that developed in the twentieth century is its remarkable distribution system that links producer and consumer. The need for speed arises because cathinone degrades within forty-eight hours of being picked from the tree or bush. This volatility is well known to producers and consumers and has shaped the development of the trade, so that rapid transportation has defined the geographical spread of markets. Khat must and does reach consumers rapidly and is transported by road and air to East African and Yemeni cities and remote hamlets. Hence, during the late twentieth century and into the new millennium khat use continued to spread throughout East Africa, in Kenya, Uganda, Rwanda, and Tanzania, where it is the drug of choice for many youth.

Somalis live all over East Africa as long-term migrants and as refugees since the war of the early 1990s. However, since that war and continuing civil unrest and the resulting dispersal of Somalis

across the world, khat has been thrust into the limelight. Khat is popularly portrayed as a dangerous substance in films such as *Blackhawk Down* (2001) and is decried, particularly by the U.S. authorities, as destructive of the Somali social fabric. Yet, khat consumption is a relatively recent cultural phenomenon for most Somalis.

Khat is also exported from Kenya, Ethiopia, and Yemen to migrants living in Europe and in North America. Hence, between 1988 and 2008 khat became a global commodity, openly on sale in London, Manchester, and Amsterdam, and covertly in New York, Toronto, Chicago, and Sydney. The development of these markets has occurred concurrently with the influx of large numbers of Somali refugees.

See also **Amphetamine.**

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SUSAN BECKERLEG

L

L-ALPHA-ACETYLMETHADOL (LAAM). Acetylmethadol (also referred to as *l*-alpha-acetylmethadol, methadyl acetate, LAAM or L-AAM) is structurally related to methadone. LAAM is a potent opioid agonist with properties similar to methadone, except for its prolonged half-life. This slow elimination can be useful clinically, since 50–80 milligram doses of LAAM given three times a week are equivalent to daily doses of 50–100 milligrams of methadone in preventing the symptoms of opioid withdrawal. Thus, addicts on maintenance treatment would need to come to a clinic only three times a week for LAAM instead of daily for methadone. Since the early 1970s, methadone has been the only agent approved for use in maintenance-treatment programs for heroin addicts, but research has shown that LAAM can be a useful alternative. In 1993, the U.S. Food and Drug Administration (FDA) initiated the legal changes needed to make LAAM available for clinical use.

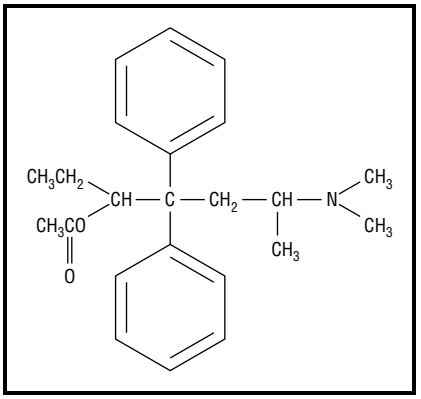

Figure 1. Chemical structure of LAAM. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Treatment, Pharmacological Approaches to: An Overview.**

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GAVRIL W. PASTERNAK

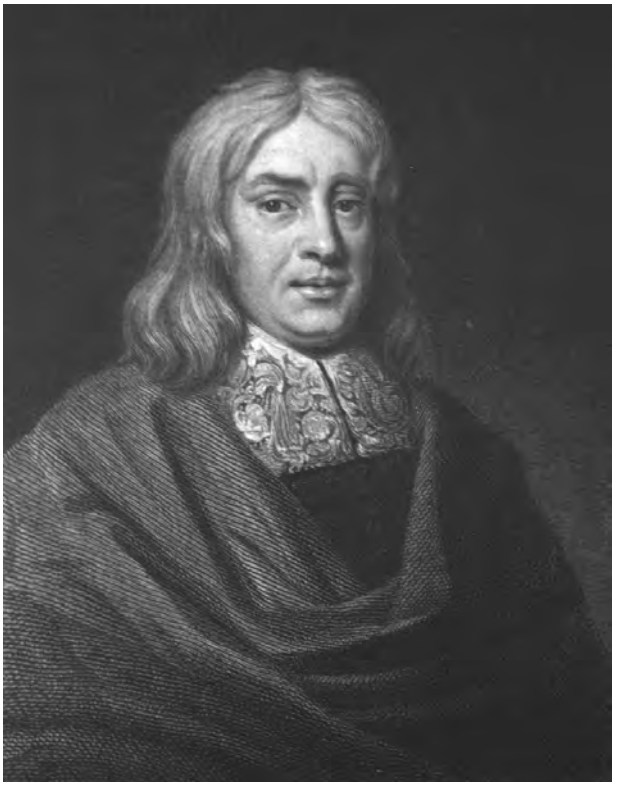
LAUDANUM. Laudanum refers to a mixture of alcohol and opium. The opium was commonly mixed with different wines or spirits and a variety of other ingredients to disguise its bitter taste. Generally, alcohol accounted for about 20 percent of the preparation. Ancient cultures made use of alcohol-based extracts of opium, and it is not uncommon to find references to such concoctions in the writings of Hippocrates, Pliny, or Dioscorides (Tainter, 1948, p. 4).

However, scholars generally agree that Paracelsus (1493–1541), a Swiss contemporary of Copernicus, Luther, and da Vinci, with knowledge of both alchemy and medicine, can be credited with the creation of laudanum. At the time of Paracelsus, many different preparations existed with varying amounts of opium and other ingredients such as gold, pearls, and a substance called laudanum (Norton, 2005, p. 147).

The final ingredient refers to a gummy plant resin that was commonly used in these medicinal preparations. Whether the resin of the rock rose (*Cistus ladanifer*) gave laudanum, the alcoholic extract of opium, its name, or whether the word *laudanum* comes from the Latin word *laudare*, to praise, is of some dispute among historians (Van Ree et al., 1999, p. 342). However, from the sixteenth century onward, the name *laudanum* was attached to mixtures containing opium (Norton, 2005, p. 147).

Different competing preparations of laudanum existed in the seventeenth century. Yet, around 1670 one of the most popular laudanum preparations was created by Thomas Sydenham (1624–1689), a British physician. Sydenham's laudanum, a liquid, is said to have replaced the solid form used before that time. Aside from opium, the laudanum pill often contained substances such as saffron, castor, ambergris, musk and nutmeg (Hodgson, 2001). From his publications, scholars learned that Sydenham used sherry wine, opium, saffron, as well as powders of cinnamon and cloves in his particular version of the preparation which he administered to treat a variety of diseases such as smallpox, gout, and dysentery (Latham, 1979; Payne, 1900, p. 182). Given the sleep-inducing qualities of opium, the mixture was also prescribed to calm patients.

While other laudanum compounds were available, Sydenham's laudanum was one of the most common forms in which opium was consumed from the eighteenth until the early twentieth century in both Europe and the United States. The substance was widely offered to the public and sold at markets and shops, through mail order and by physicians. In the United Kingdom, the use of laudanum cut across different social classes. Wealthy gentlemen and their wives as well as the working class poor consumed it (Berridge, 1978, pp. 108–109). In the United States, however, historians suggest laudanum use was more an upper and middle class phenomenon with women using the substance disproportionately in comparison to their male counterparts (Courtwright, 2001, pp. 36–37).



Thomas Sydenham. ENGRAVED BY EDWARD SCRIVEN. THE LIBRARY OF CONGRESS.

In many ways, laudanum was the cure-all medicine of the practicing physician in the eighteenth and nineteenth century who had limited remedies available for prescription. All types of diarrheal diseases were treated with laudanum because of opium's antiperistaltic, constipating effect. Laudanum was also administered to treat cholera, rheumatism, and tuberculosis; to suppress coughing; and to alleviate respiratory diseases. For individuals with sleep disorders, laudanum was a standard part of any treatment regimen (Duffy, 1993, pp. 180–181). Medical journals of the mid-nineteenth century report that laudanum was also used to fight alcohol-induced delirium tremens and as an antidote to arsenic poisoning (Ryan, 1845).

During the Seminole Indian Wars (1817–1818; 1835–1842; 1855–1858) as well as during

the American Civil War (1861–1865) laudanum was given to wounded soldiers before they underwent amputations and to alleviate pain in general. It was also used to treat fevers and was given in large doses to cure diarrheal diseases. Both fever and dysentery were common afflictions of soldiers due to the state of their living conditions and frequent malnutrition (Straight, 1978, p. 633; Courtwright, 2001, p. 54).

Laudanum was so readily available throughout the eighteenth and nineteenth century that Americans as well as Europeans used the substance not only to treat their ailments but also to commit suicide (Clarke, 1985, p. 238). If shop owners were not willing to sell large quantities of laudanum, people would go to several sellers to procure a sufficient amount or invent convincing stories that would sway the shop owner. Pretending that the laudanum was for external applications or claiming that the preparation would be used for animals were successful ways to obtain large quantities. Stories of accidental poisoning were equally common, and children often suffered the consequences of an overzealous caregiver who sought to quiet a restless child or treat some other childhood disease by administering laudanum (Everest, 1842; Herapath, 1852; 1853). Overuse and abuse of laudanum and similar preparations was common.

According to the American Pharmacists Association, opium mixtures are controlled substances in the United States and only used to treat severe diarrheal diseases. Present-day compounds contain approximately 10 milligrams of anhydrous morphine per milliliter. Additionally, diluted opium mixtures are used to treat and alleviate withdrawal symptoms in neonates whose mothers were addicted to opioids during their pregnancies. Having recognized the abuse potential and risk of opioids, the Federal Drug Enforcement Administration rated laudanum a Schedule II drug. Laudanum has been tested as an alternative to methadone maintenance and the results from France were encouraging (Auriacombe et al., 1994 p. 567).

Laudanum should not be mistaken for its much weaker cousin, paregoric. Paregoric is a camphorated opium preparation, widely used in the eighteenth and nineteenth century to alleviate diarrheal diseases and infant colic. The mixture contains approximately 4 milligrams anhydrous morphine per 10 milliliters (Loyd, 1997, pp. 428–429). In the twenty-first century, paregoric is rated a Schedule III drug with medicinal use and less abuse potential than laudanum.

See also **Morphine; Nutmeg; Opiates/Opioids; Opioid Complications and Withdrawal; Pain, Drugs Used for; Paregoric.**

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AUKJE KLUGE

LD50. In preclinical studies, the LD50 is the median lethal dose—the dose of a drug that produces death in 50 percent of the experimental animals tested. The LD50 can be estimated from a dose-effect curve, where the concentration of the drug is plotted against the percentage of animals that die. The ratio of the LD50 to the ED50 (the median effective dose) indicates the therapeutic index of a drug for that effect and suggests how selective the drug is in producing its desired effects. In clinical studies, the concentration of the drug required to produce toxic effects can be compared to the concentration required for therapeutic effects in the population to estimate the clinical therapeutic index.

See also **Research, Animal Model: An Overview of Drug Abuse.**

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NICK E. GOEDERS

LEDERMANN MODEL OF ALCOHOL CONSUMPTION. *See* **Prevention of Alcohol Related Harm: The Total Consumption Model.**

LEGAL REGULATION OF DRUGS AND ALCOHOL. Legal regulation can be used in four general ways to influence the incidence, prevalence, patterns, and circumstances of consumption of potentially harmful substances, including alcohol, tobacco, and other drugs. The most direct mode of legal intervention is to establish the conditions under which a potentially harmful substance is available. In doing so, the law can employ either a *prohibitory scheme* that prohibits the production or distribution of the substance for nonmedical or self-defined uses, or a *regulatory regime* that permits the substance to be lawfully available for nonmedical or self-defined uses but that may regulate the product, its price, and the conditions under which it is accessible.

A completely successful prohibition would prevent any nonmedical consumption of the proscribed substance; however, the more likely consequence of a prohibitory scheme is that an illicit distribution system will arise to respond to whatever demand exists for the substance. In that case, the manner in which the prohibition is enforced can also influence the product, its price, and the conditions under which it is available.

A second mode of legal regulation is to regulate the flow of information and messages regarding use of the particular substance. The government may

initiate its own informational efforts to influence attitudes, beliefs, and behavior. Government may also attempt to influence private communications, either by proscribing certain messages altogether or by regulating or restricting their content. Such restrictions have generally taken two forms: mandatory warnings and proscriptions of certain types of messages.

A third mode of legal control is the direct regulation of consumption, either by proscribing and imposing sanctions for undesired behavior or by withholding benefits or privileges to which the individual would otherwise be entitled. Thus, the law may proscribe use of a substance altogether, or it may prohibit such behavior in certain specified circumstances. Examples of total bans include unauthorized possession and consumption of controlled substances and consumption of alcohol by persons under the minimum age. Situational prohibitions include laws against consuming alcohol or smoking tobacco in public areas. Laws that require drug testing of workers and that permit job termination or discipline as a consequence of a positive test illustrate less coercive measures of deterrence.

A fourth use of the law emphasizes its declarative aspects. Whether a legal control has a direct impact on the marketplace or on the prevalence of the disapproved behavior, it may symbolize and express the official government view of the behavior and may generate derivative effects on behavioral patterns by influencing attitudes and beliefs. To the extent that citizens customarily defer to and respect the law or are influenced by messages of official approval or disapproval, a declaration of illegality may serve an educative, or didactic, role. Specification of a minimum drinking age, regulation of the availability of drug paraphernalia, and sanctions for possession of illicit drugs may all generate these symbolic effects, even if the direct effects tend to be modest.

AVAILABILITY

The National Commission on Marihuana and Drug Abuse identified four models of availability for psychoactive substances: The first involves no special controls at all; the substance is treated in the same way as other unregulated market commodities. Under the second approach, the substance is subject to special controls but remains lawfully available for self-defined or nonmedical purposes. The third model limits availability to specific purposes, generally to medical and research uses only. Under the fourth approach, the substance is not legally available at all except perhaps for narrowly circumscribed use in research. The first two models can be characterized as regulatory approaches (because the substance is legitimately available for nonmedical or self-defined purposes) and the second two as prohibitory approaches (because the substance is not available for self-defined or nonmedical purposes). Tobacco and alcohol are lawfully available for nonmedical uses, but they are subject to variable regulatory controls designed to affect the product, place, and conditions of consumption. (Only the solvents and inhalants—glue, lacquer, thinner, ether, gasoline, nitrous oxide—are essentially uncontrolled.) However, most psychoactive substances (legally denominated controlled substances) are subject to prohibitory controls, which means their availability is limited by law to medical and research uses. One minor exception among psychoactive substances is peyote, which is available to members of the Native American Church for sacramental uses.

Alcohol. The availability of alcohol is governed by alcoholic beverage controls (ABC) that vary from state to state. ABC agencies view their primary responsibilities as providing an orderly market for the distribution of alcoholic beverages, controlling criminal involvement in the market, and generating tax revenues. Since the 1960s, the trend has been to liberalize restrictions on access to, and availability of, alcohol in order to facilitate private choice, to protect commercial interests, and to raise revenue. Only since the late 1980s have some ABC agencies shown any inclination to use their regulatory authority to influence the prevalence pattern and circumstances of consumption. Relevant aspects of ABC regulation include pricing and/or taxation policies, zoning, and rules regarding hours and days of sale.

Direct regulation, under the authority of ABC boards, is not the only method by which the law can influence the conditions under which alcohol is available. For example, one way to discourage retail sellers of alcohol from selling the substance to a person already intoxicated is to hold them legally liable for injuries subsequently caused by the

intoxicated consumer, even after the consumer leaves the premises. Although the legal theory has changed over the years, the risk of liability for commercial suppliers under so-called dramshop liability laws is relatively well established. Moreover, the courts of several states have extended liability to the hosts of social events who served alcohol to obviously intoxicated guests who then cause injuries in their intoxicated condition.

Tobacco. For the most part, the public health dimensions of tobacco regulation have been reflected only in product, package, and advertising requirements designed to facilitate informed consumer choice. Only since the late 1980s has the federal government moved toward a policy that unequivocally establishes reduced consumption as its goal. Although a national prohibition is unlikely in the foreseeable future, several regulatory initiatives are being undertaken at all levels of government. For example, states will not receive federal money for mental health and substance-abuse services, unless they implement a plan for enforcing bans against the distribution of tobacco products to minors. Many localities have banned tobacco product vending machines. In addition, several states have raised cigarette excise taxes with the aim of reducing consumption, and the federal excise tax has been increased by a substantial amount, with the dual aims of reducing smoking and raising revenue.

In 1996, the U.S. Food and Drug Administration (FDA) asserted jurisdiction over traditional tobacco products under the Food, Drug, and Cosmetic Act, on the theory that tobacco products are intentionally marketed to satisfy consumers' addiction to nicotine. Based on this interpretation of the act, the FDA adopted regulations prohibiting the distribution of tobacco products to minors and, as discussed below, restricting the marketing of tobacco products to youths. However, the U.S. Supreme Court ruled in 2000 that the FDA did not have jurisdiction over traditional tobacco products under existing law and Congress had declined to confer such authority as of 2008.

In addition, smokers or their survivors have sued tobacco companies, with mixed success, seeking damages for smoking-induced disease or death. In 1998 the major tobacco companies entered into a Master Settlement Agreement with the state attorneys general, agreeing to pay $246 billion to the states over the duration of twenty-five years to settle lawsuits seeking to recover the states' costs of treating smoking-related diseases. Obviously, imposing liability on manufacturers for the adverse health consequences of smoking can have a major impact on the economics of the industry. In this instance, the indirect regulation of tobacco by the tort system has exerted a more potent influence on industry behavior than many direct regulatory alternatives, such as pricing policies, outlet limitations, or tar and nicotine limitations.

Controlled Substances. The manufacture and distribution of opiates, cocaine, cannabis (marijuana), stimulants, depressants, and hallucinogenic substances outside medical and scientific channels are unlawful under both federal and state controlled substance laws. The production and distribution of these substances within medical and scientific channels are subject to varied levels of restrictions based on their potential for abuse and their level of accepted medical use under the Controlled Substances Act of 1970. The wisdom of these prohibitions, especially in relation to cannabis, has been questioned by some on the grounds that the suppression of nonmedical use is not a legitimate governmental objective, and if it is, then the costs of the prohibitions exceed the benefits of the reduced consumption they achieve.

A particularly controversial aspect of cannabis regulation has been its classification as a Schedule I drug under the Federal Controlled Substances Act and its state counterparts. Schedule I is the most restrictive classification, reserved for drugs without any accepted medical use. Critics of the law have argued that marijuana is medically useful to treat glaucoma, AIDS wasting syndromes, and other conditions. Eleven states have adopted laws that legitimize bonafide medical uses under state law. These laws have created the unusual situation in which any effort to make marijuana available for medical uses could be prosecuted as a violation of federal law. The Supreme Court ruled in 2001 that anyone distributing medical marijuana could be prosecuted under the Federal Controlled Substances Act, and in 2005 extended this ruling further by holding that users of medical marijuana could be prosecuted under the act. However, the federal government has not moved aggressively to initiate such prosecutions. The

Institute of Medicine of the National Academy of Sciences has identified promising avenues of therapeutic use for the active constituents of cannabis and has recommended further research.

INFORMATION REGULATION

A government aiming to discourage what it perceives as unhealthy or unsafe behavior is not likely to be satisfied with the influence of its own messages and may seek to regulate communication by others within the bounds of the First Amendment, which protects freedom of speech. This can be done in two ways. First, the government may require individuals or organizations to convey the government's desired message. Laws requiring product manufacturers to include information on or with their products have become a standard feature of health and safety regulation. Mandatory package warnings have been used as a means of informing consumers about the dangers of tobacco and, more recently, of alcohol use. Second, government may ban communication of messages that it regards as undesirable. For example, laws banning false or misleading advertising are common, but government may choose to go a step further and suppress a message because it is thought to encourage unhealthy or socially disapproved drug, alcohol, or tobacco-using behaviors. Examples include the federal ban on broadcast advertising of cigarettes and state laws that ban alcohol advertising. Public-health advocates have urged the federal government to prohibit all forms of tobacco advertising. Whether such prohibitions actually affect the level of consumption (as opposed to product choice) remains controversial. The FDA 1996 Tobacco Rule, which was invalidated by the Supreme Court in 2000, would have restricted the advertising of tobacco products to a text-only format and would also have banned other forms of promotional activity that are thought to make use of tobacco products attractive to children and adolescents. The tobacco companies agreed to abide by some of these marketing restrictions in the Master Settlement Agreement executed in connection with the suit brought by the attorney generals of these states.

Proposals have also been made to move beyond advertising into the area of entertainment programming, eliminating messages that portray smoking and drinking in an attractive way. Clearly, such initiatives would raise serious constitutional questions concerning free speech.

Governments have also occasionally attempted to purge the environment of messages that are thought to encourage illicit drug use. For example, one provision of the Model Drug Paraphernalia Act (drafted by the federal Drug Enforcement Administration as a model for states to enact) specifically bans paraphernalia advertising. In 1973, the Federal Communications Commission (FCC) threatened to revoke the licenses of radio stations whose lyrics were thought to encourage illicit drug use.

DIRECT REGULATION OF CONSUMER BEHAVIOR

A decision to discourage nonmedical drug use—and to proscribe transactions outside medical channels in order to restrict availability for such use—does not necessarily entail a decision to proscribe and punish unauthorized consumption. Values of individual freedom weigh very differently in the two contexts.

From the perspective of libertarian philosophy, it has been argued that the criminalization of private use (and possession for such use) of drugs is categorically illegitimate, and the criminal prohibition should be limited to behavior that endangers others. This position leads to a discussion of the ways in which drug use might affect others. Even if criminalization is not categorically objectionable, the costs of it may exceed the benefits. The National Commission on Marihuana and Drug Abuse relied on such a cost-benefit assessment in 1972 when it recommended the decriminalization of possession of marijuana for personal use. A few states have decriminalized the possession of marijuana, although they have usually substituted a civil fine. Some of the states that took this action subsequently recriminalized the possession. Aside from marijuana, possession of all other controlled substances is a criminal offense in all states as well as under federal law. In addition, the possession of alcohol by underage consumers is an offense in most states. Even if the possession or use of a substance is not categorically proscribed, prohibitions can be used to deter and punish socially harmful behavior or to provide leverage to coerce individuals into treatment. Public smoking laws and laws prohibiting driving while intoxicated (or while having a

Under the Federal Controlled Substances Act, marijuana is categorized as a Schedule I drug, the most restrictive classification. Opponents of its labeling maintain that marijuana is effective in managing some medical conditions. CANADIAN PRESS/PHOTOTAKE

certain level of blood alcohol content) provide the prime examples.

DECLARATION ASPECTS OF LEGAL REGULATION

Government sends messages by its actions as well as its words. By declaring conduct illegal or by using any of the other instruments of legal intervention described above, the government expresses and formalizes social norms. However, knowledge of the official preferences may actually encourage the disapproved behavior among disaffected, outsider groups. Measuring such symbolic effects is difficult because of the need to isolate these hypothesized effects from other influences on attitudes and beliefs.

Arguments drawing on the declarative aspects of legal regulation are routinely employed by proponents of restrictive controls over the availability and consumption of alcohol, tobacco, and other drugs. Criminal sanctions against the simple possession of controlled substances are frequently regarded as indispensable symbols of social disapproval. Such arguments have been prominent in debates concerning the decriminalization of marijuana possession. Moreover, graded or stratified penalty schemes, which punish the possession of more harmful drugs more severely than that of less harmful drugs, may be favored because they denote the relative seriousness of these transgressions. Public smoking bans and antiparaphernalia laws seem to be particularly designed to reinforce attitudes unfavorable to smoking and recreational drug use.

Statements of legal rules can serve an educational role even if they do not penalize the

undesired behavior. Minimum-drinking-age laws (which prohibit the distribution of alcohol to youth) provide a good example because they denote the norm even if the youthful drinker is not punished. Similarly, bans on alcohol or tobacco advertising might be enacted to erase a possible symbol of social approval, even if the proponents did not believe that such bans would directly reduce consumption.

See also **Advertising and the Alcohol Industry; Advertising and the Pharmaceutical Industry; Alcohol: History of Drinking in the United States; Dramshop Liability Laws; Legalization vs. Prohibition of Drugs: Policy Analysis; Minimum Drinking Age Laws; Opiates/Opioids; Parent Movement, The; Tobacco, Advertising and.**

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LEGALIZATION VS. PROHIBITION OF DRUGS: HISTORICAL PERSPECTIVE.

The history of U.S. social and legal policy in regard to psychoactive and intoxicating drug use has been characterized by periodic shifts, strong ideological presuppositions, and deep disappointment. Any analysis of current policy and the debate about drug legalization must recognize the historical roots of current policy that affect the various positions in the debate.

A brief historical note may help place the current discussion of drug policy in the United States in perspective. To borrow a phrase from Ecclesiastes, there is nothing new under the sun. Those engaged in the current, often heated, discussions about national drug policy often act as if their concerns, insights, and positions about intoxication, drug use, and society are unique to the twenty-first century. A cursory review of history indicates that the debate on the meaning and effects of alcohol and other drug use on morals, public safety, productivity, and health is at least as old as written language. Some of the earliest recorded civilizations struggled with the issue and often adopted laws and policies that attempted to regulate strictly or prohibit the use of alcohol and other drugs.

Often these laws were based on a culture's perspective on the will of the divine or combined with basic civil codes. For example, the Torah appears to be very concerned with excessive alcohol use. It was seen as leading to gross immorality. The Christian New Testament holds similar views, particularly on the excess use of alcohol. The theme seems to be one of avoiding all things that harm the body or one's relationship with God, and moderation even in all things that are good. The Qur'an takes a very strong prohibition stand against alcohol and all intoxicating substances. Since much of modern Western civilization derives from these religious traditions, they continue to influence public thinking and policy. From a less theocentric perspective, many ancient civil codes also struggled with the regulation or prohibition of intoxicating chemicals. For example, the Romans seemed especially concerned that slaves and women not use alcohol and forbade its use by them. The concern appeared to be that alcohol would make slaves less productive and more difficult to control and that it would also lead to female sexual impurity. Chinese emperors prohibited the use of opium among their subjects. In addition, during the sixteenth and seventeenth centuries, when tobacco use began to spread around the world, many societies, including

the Ottoman Empire, Great Britain, Russia, and Japan, initially tried prohibiting the substance.

These ancient and more recent laws and codes show that the regulation or prohibition of socially perceived harmful substances is not new to the twenty-first century, nor is the range of views on the negative consequences of regulation or prohibition and what would constitute a more effective, less harmful policy.

PHILOSOPHICAL AND CULTURAL TRADITIONS

Among the many legacies that underpin the present discussion of drug policy in contemporary society are four at times overlapping and sometimes contradicting philosophical and cultural traditions. The first is the basic American heritage of individual liberty and limited government interference with any variety of human choice, even if that choice is harmful to the individual making the decision and morally repugnant to the majority of society. This position was eloquently argued by British philosopher and economist John Stuart Mill (1806–1873) in his essay *On Liberty* (1859).

A second major social tradition is rooted in the moral utilitarian view of government that is also a part of the nation's heritage. The utilitarian perspective, also argued by Mill in his book *Utilitarianism* (1863), emphasized that government has a legitimate right to prohibit the behaviors that actually cause real harm to others. From this viewpoint, government has the right and responsibility to protect the common welfare by legally prohibiting individuals from engaging in behavior that is demonstrably harmful, not to themselves (which would have been an interference with liberty), but to other citizens.

The moral utilitarian perspective was an important underlying element in many of the late nineteenth- and early twentieth-century social-reform movements that culminated in the many state laws prohibiting narcotics and other drug use, the national Harrison Narcotics Act of 1914 and the Volstead Alcohol Prohibition Act of 1920. The utilitarian perspective was that narcotics and alcohol use caused real harm to others and society in general in the form of family poverty, crime, violence, and health-care costs.

A third social tradition that has influenced U.S. drug policy is commercialism (Courtwright, 2001). There is ample evidence that through the nineteenth century, U.S. society had a strong commercial attitude toward alcohol use and the use of a variety of powerful drugs. As has been documented by historians, merchandise catalogs and traveling entrepreneurs legally distributed opium, barbiturates, and cocaine as wonderful cure-alls for the ills of the human condition (e.g., Spillane, 2000). These merchants were an organized, respected part of the commercial establishment. Perhaps based on British narcotics commercialism, there has always been a commercial attitude toward alcohol and drug distribution in the United States. From the commercial perspective, alcohol and drugs are a wonderful commodity. They are often rapidly metabolized, highly addictive, and easily distributed. However, by the end of the nineteenth century, this rather freewheeling distribution of drugs caused a widespread public reaction that became incorporated into a variety of health- and social-reform movements.

A fourth significant element in the development of national alcohol and drug policy is a public health perspective. As was noted, at the turn of the twentieth century the United States was in the midst of major social and health reforms. After the passage of the 1906 Pure Food and Drug Act, a host of public-health-based government bureaus and regulations emerged, focusing on improving the quality of meats and other foods and requiring the accurate labeling of drugs. In addition, the American Medical Association initiated major reforms in the medical profession, eliminating over-the-counter narcotic drug advertisements in their journal and supporting the licensing of physicians as the only legitimate prescribers of many drugs. The public-health reform movements attempted to de-commercialize drug distribution and make drug use a medical, not commercial, decision. The passage of the Harrison and Volstead Acts probably represented a significant triumph of the moral utilitarian and public-health perspectives.

Following the Harrison Act and further legislation, the U.S. government instituted various bureaus and departments to carry out law enforcement and antidrug educational programs. Any review of the education programs of the Bureau

of Narcotics would tend to conclude that they primarily constituted a heavy dose of propaganda with little basis in scientific fact. The federal proclivity for restricting the availability of drugs and arresting users and dealers continued strongly through the 1960s. During the decades following the Harrison Act and until the 1960s, the media and government were fairly united in their opposition to drug use, and there were few questions about the efficacy of drug laws or the social policy on which those laws were based.

THE 1960S AND 1970S

In the 1960s, U.S. society experienced the coming of age of the first of the baby boomers—those born between 1946 and 1960. By their sheer numbers, a proportion of this generation challenged the traditional socialization mechanisms of society and significantly questioned traditional assumptions, rationales, explanations, and authority. In a drive for generational self-discovery, drug use, particularly as a means to alter consciousness, became a part of the youth movement of the late 1960s and the 1970s. Most of the baby boomers who used drugs explored the use of marijuana and hallucinogens, but over the same years heroin use was increasing in inner cities across the country; crime, too, was increasing. Despite the declaration of a "war on drugs" by the Nixon administration from 1970 through 1971, national surveys conducted during the 1970s and early 1980s showed annual increases in almost all types of drug use among high school seniors, household residents, and criminal justice populations. The one exception was heroin, the major target of the Nixon drug war. Heroin use levels declined and then remained stable, but cocaine use rose dramatically during the 1970s and early 1980s, as did marijuana use among young people. By 1985, more than 20 percent of U.S. adults had taken drugs illegally, and for persons aged eighteen to thirty-four more than 50 percent had done so.

Perhaps because of the fundamental changes in national drug-using behavior that occurred during this period, the modern movement to legalize drugs began. The basis of the argument was that (1) many of the drugs that were then illegal were not as harmful as government and media propaganda portrayed them to be, (2) marijuana in particular was argued to be relatively less harmful than alcohol and tobacco, and (3) the use of marijuana was a generational choice. In fact, the 1978 National High School Senior Survey showed that in the prior thirty days, a higher proportion of seniors had smoked marijuana than had smoked tobacco. By 1979, the media and American households were holding serious discussion about the legalization of marijuana, moving toward the British System of heroin maintenance, and considering the legalization of cocaine as a nonaddictive stimulant. Social political movements such as NORML were organized to achieve passage of laws decriminalizing marijuana use. With the tacit support of the Carter administration, there were eleven states, including Alaska, that decriminalized the possession of small amounts of marijuana for personal use. Even the director of the National Institute on Drug Abuse in the late 1970s, Robert Dupont, appeared to accept the likelihood that marijuana would be decriminalized. However, in 1977, in reaction to growing marijuana use by young people and a perception that government itself was being tolerant of drug use, groups of parents organized a grassroots campaign to buttress the resistance to drug law liberalization. By 1978, the Parents Movement had become a force to be considered, and their views had ready access to the White House policy office. The apparently about-to-be-successful national movement to legalize many drugs in the 1970s came to an abrupt end with the 1980 election of President Ronald W. Reagan.

THE 1980S

Corresponding with the election of President Reagan, there was a general conservative shift in national consciousness. First Lady Nancy Reagan, who made drug use among young people one of her prime topics of concern, was a welcome speaker at annual national meetings of the parents' groups. The public debate on legalization during the early 1980s was also affected by increasing evidence of the physical and psychological consequences of drug use, declining illegal drug use among high school students, decreasing use among household members, and, maybe, the initiation of maturation among the baby boomers. During the 1980s, U.S. policy was characterized by the increasing intolerance of drug addiction or even recreational drug use. On an official level, this came to be called *zero tolerance.*

According to the official federal policy of the 1980s, the assumption was that to a large extent drug use was an individual choice that could be affected by raising the cost of drug use to the users. It was believed that if enforcement reduced the availability of drugs, thus raising their prices, and increased the consequences of use by increasing the severity and certainty of punishment, individuals would choose to say no to illegal drug use. During the 1980s, the proportion of federal drug control spending allocated to treatment fell from 33 percent in 1981 to just 17 percent in 1992, with increasing shares going to prevention (up from 8% to 14%) and law enforcement (up from 59% to 69%). The increase in the overall size of the federal budget was even more dramatic. The total federal budget for all demand-side and supply-control activities was just $1.9 billion in 1981. This amount escalated sharply when President Reagan redeclared a war on drugs. By 1989, the total had reached $6.7 billion. The resources escalated still further during the Bush Sr. and Clinton administrations, reaching $12.2 billion in fiscal year 1993 and $18.1 billion in fiscal year 2001. (Direct comparisons with more recent budgets are complicated by definitional changes, but federal drug spending during the George W. Bush administrations has grown by an average of only 2 percent per year in real terms.)

By the end of the 1980s, the national drug-abuse policy of zero tolerance with a heavy focus on enforcement began receiving critical reviews from policymakers, public administrators, clinicians, and academic researchers. These critical reviews were generally based on civil libertarian and public health harm-reduction perspectives. The key points made by national policy critics were:

1. About two-thirds of all felony arrestees in major metropolitan areas were currently using cocaine.
2. A large proportion of all criminal charges were drug charges. This had resulted in a significant expansion of prisons and the proportion of the population incarcerated. All this had occurred at a very high economic cost.
3. The high profits from the drug trade were funding international terrorism and resulting in a rapidly increasing rate of violence in American urban areas.
4. Because of the vast amount of cash generated in the drug trade, there was great potential for corruption of government.
5. In an attempt to reduce illegal drug use, draconian laws focusing on search and property seizures had been passed.
6. Treatment availability for the poor had been reduced, with many cities reporting month-long waiting lists for publicly funded treatment slots.

CALLS FOR DECRIMINALIZATION

These consequences resulted in a major reinvigoration of the interest in legalizing or decriminalizing drug use. Those who argue for legalization come from a wide variety of professions and ideological positions, but they all essentially believe that U.S. society has reached the point where it can no longer afford to enforce existing law. There simply are not enough police, courts, prosecutors, or jail cells, nor is there the sense of justice that will allow U.S. society to enforce laws that have been broken by more than 20 percent of U.S. citizens.

In summary, the zero-tolerance, just-say-no policy of the 1980s had come to be viewed by critics as resulting in a virtual saturation of the criminal justice and prison system with drug law offenders, the undermining of crucial civil rights, and the decreasing availability of drug treatment for the poor accompanied by increasing violence in high drug-trafficking areas and large-scale public corruption. Many critics came to view drug laws as contrary to the very basis of a libertarian civil government. These critics saw the war on drugs declared in the 1980s and continued to the present as inimical to civil liberty. In addition to the civil libertarian perspective, there are many critics of current drug-prohibition policy who focus on a public-health harm-reduction perspective. From this perspective, current policy is not reducing the public-health harm caused by drug use. The public-health-reduction model emphasizes that drug abuse and addiction are the product of a complex set of psychological, sociological, and economic variables that are very little affected by the threat of prison. This perspective argues that the best way to reduce the personal and public-health harm of

drug use would be to increase drug education and prevention, increase drug-treatment availability, and reduce the harm caused by drug abuse by providing clean needles and, perhaps, decriminalizing use—thus significantly reducing the cost of drugs and the associated crime.

Although there are very few detailed legalization proposals, those who advocate decriminalization generally argue that national policy should move toward an approach in which the distribution of drugs such as marijuana, cocaine, and heroin would not be governed by criminal law but by governmental regulations that controlled the manufacture, distribution, and use of these substances so that they would go only to those already addicted or be dispensed under very regulated conditions. Advocates of this policy believe that the movement of drug policy from criminal law to regulatory restrictions would result in the relatively easy availability of drugs and inexpensive access to them for those who are addicted, thus resulting in a significant reduction in corruption and violence as well as an increasing willingness on the part of addicts to enter treatment. This, it is asserted, would relieve the severe overcrowding of the criminal justice system. At the same time, it is argued, because of strict regulation, this policy change would more effectively protect young people as well as public health and safety than the current policy (Nadelmann, 1988; Wisotsky, 1991).

OPPOSITION TO LEGALIZATION

Critics of the legalization perspective do not question many of the basic judgments of the consequences of the 1980s national policy, but they do severely question the assumptions on which legalization is based. Those who are opposed to drug legalization often draw on the moral utilitarian and public-health perspectives. They make the following arguments:

1. During the 1980s and continuing into the 2000s, drug use, by all measures, significantly decreased among high school and college students as well as in the general population.
2. It is naive to assume that increasing availability, lowering cost, and reducing legal consequences will have no effect on the incidence and prevalence of marijuana, cocaine, and heroin use. From this perspective, it is argued that once these drugs are legalized, even though regulated, they will enter the arena of advocacy through free speech and thus the realm of market creation and expansion through advertising. Alcohol use, which is severely regulated and illegal for those under twenty-one years of age, is initiated in junior high school. In addition, about one-third of high school seniors report being drunk each month. In most states, tobacco cannot be sold to minors, but smoking among junior high school students is common. These facts imply that regulation to make a drug available to one age group actually makes it available to all age groups.
3. The resulting increase in use in society and broadening of the societal base of use will result in detrimental health, behavioral, and economic consequences that will far outweigh any proposed benefit of legalization.
4. There is no broad societal base for legalizing drugs. Surveys among high school seniors clearly show that a large majority oppose the legalization of drugs—even the legalization of marijuana. Traditionally liberal countries such as Switzerland and Sweden have tried relaxing drug laws and were forced to modify their positions by their citizens, who daily had to experience the consequences of wide drug availability. Additionally, in a referendum in November 1991, Alaskans voted to rescind a marijuana legalization law passed in the 1970s and recriminalized marijuana possession. In a democracy, governmental policy cannot ignore the voice of the public. Dr. Joycelyn Elders, the first Surgeon General in the Clinton administration, was criticized for merely suggesting that the issue of legalization should be debated.
5. Although the costs of drug law enforcement and incarceration of offenders may seem high, it is a misconception to assume that those incarcerated are all petty first-time violators of the drug laws. DiIulio (1993) asserts that "in 1991 more than 93 percent of all state prisoners were violent offenders, repeat offenders (one or more prior felony convictions) or violent repeat offenders." Likewise, most drug-related violators in prison are not just users

but played some (perhaps minor) role in drug distribution. For many the official conviction charge is "possession," but that includes possession with intent to distribute, those who pled down from a trafficking charge, and couriers who possessed very large quantities.

Many of those opposed to legalizing drugs, such as former Secretary of Health, Education and Welfare Joseph A. Califano, Jr., and Mathea Falco, a former Carter administration official, argue that the existing policy should be drastically modified to increase the availability of treatment and educational and economic opportunities in societal groups with high drug-use rates. Specifically, what is called for is an increase in treatment availability in the criminal justice system, either through diversion or probation to treatment or through the provision of therapeutic services in jails and prisons, as well as a major increase in the availability of publicly funded treatment slots in the United States. Policy analysis studies began to conclude that every dollar invested in treatment results in several dollars saved in terms of other social costs, including crime (e.g., Rydell and Everingham, 1995; Gerstein et al., 1994).

Some who oppose drug legalization believe that the current discussion has subtly eroded the public's will to fight illegal drug use. From this perspective, the only way to retain the reduction in general societal drug use that occurred during the 1980s is to retain a vigorous enforcement of drug laws. The advocates of strict law enforcement believe that weakening the war on drugs would be a kind of backdoor legitimization, a demoralizing discussion of the failure of drug policy. Previous drug policy leaders such as William J. Bennett argue that national drug policy during the 1980s was effective in reducing drug use in the general youth and adult population by making use morally, socially, and legally unacceptable and that the drug policy reform debate of the 1990s made drug use more acceptable, resulting in subsequent increases in use (Bennett & Walters, 1995a, 1995b; Rosenthal, 1995).

THE 1990S AND BEYOND

In the mid-1990s it was very difficult to reconcile the extremes of the drug legalization debate, beyond some shared belief in the need for increasing drug education, prevention, and treatment availability. However, as drug problems in the U.S. stabilized and in some cases began to ebb, the stridency of the debate has eased. Drug law reform groups have focused attention on medical marijuana, not across the board legalization, and even the famously severe federal mandatory minimum cocaine sentences and notorious New York State Rockefeller drug laws have been modified. Local drug enforcement has put greater emphasis on controlling drug-related firearms, violence, and disorder through specific deterrence and focused crackdowns, rather than trying to suppress all forms of drug selling and use (e.g., Braga et al., 2001). In many jurisdictions, law enforcement has pushed back underground, for example, to discrete sales arranged by cell phone, resulting in greatly improved quality of life in surrounding communities. Also promising are partnership efforts such as drug courts, drug offender diversion programs including California's Proposition 36, and Hawaii's very successful Opportunities for Probation with Enforcement (HOPE) coerced abstinence program (Belenko, 1999; Hawken, 2006; Kleiman, 1997). These developments might give an optimist hope that, freed to some extent from the distraction of unrealistic "silver bullet" solutions ("create a drug-free America" or "just legalize drugs"), there is potential for a more constructive period of improving drug policy bit by bit through the hard work of pragmatic policy analysis and good governance.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Crime and Drugs; Harm Reduction; Legalization vs. Prohibition of Drugs: Policy Analysis; Opiates/Opioids; Prevention, Education and; Prohibition of Alcohol; Switzerland; Temperance Movement; U.S. Government Agencies; Zero Tolerance.**

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LEGALIZATION VS. PROHIBITION OF DRUGS: POLICY ANALYSIS.

Whether a drug should be prohibited or legalized is perhaps the most fundamental question in drug policy. It is a moderately complex question and most who write about the issue do so from an advocacy perspective, so the debate is even more confusing than it needs to be. It is important to start with a clear definition of what is meant by legalization versus prohibition. There is a spectrum of policy positions. Some drugs can be used for medical but not recreational purposes (e.g., cocaine), whereas others cannot even be used for medical purposes (e.g., heroin). Some drugs cannot be used recreationally but are legal with a prescription (Valium) or when taken under medical supervision (methadone). Some drugs are legal only for adults (alcohol); others are legal for all ages (e.g., the caffeine in soda).

DIFFERENTIATING LEGALIZATION FROM PROHIBITION

When a sharp line needs to be drawn between legalization and prohibition, it is useful to say that a drug is legal if it is legal for that substance to be produced and distributed for unsupervised consumption by a significant portion of the population (e.g., all adults). By this definition making marijuana available for medical use is not legalization if prescriptions are restricted to those experiencing specific, medically diagnosed conditions (e.g., glaucoma), but it would be if any individual could write his or her own prescription. Likewise by this

definition the Netherlands has legalized retail distribution, and use of marijuana, although wholesale (large-volume) marijuana production and distribution is still prohibited. Most other drugs in most countries are either clearly legal or clearly prohibited by this definition.

DIFFERENT CRITERIA

Having defined prohibition as compared to legalization, the next important observation is that different people use different criteria for deciding what policy should be. Some people are implicitly if not explicitly consequentialists. They think the right policy is the policy that leads to the fewest problems. Others believe that there is a moral imperative to make substances legal (e.g., libertarians who believe people should be free to consume anything, even if it hurts them) or prohibited (e.g., people who believe the substance is evil for religious reasons) regardless of the consequences.

The challenge for the moral prohibitionists is defending to others why they favor prohibiting some drugs but not others. There are defensible positions predicated on consistent principles ("all intoxication is immoral" or "being physically dependent on a drug is idolatry"), but it is hard to articulate such a defense for U.S. policy. Cigarettes are highly addictive, and alcohol is clearly an intoxicant, but they are both legal. In 1930, alcohol was prohibited, but marijuana was not. Ten years later, marijuana was prohibited, but alcohol was not. One does not have to be very cynical to believe that the moral distinctions enshrined in public policy are just the legal formalization of arbitrary popular prejudices.

The challenge for the libertarian view is less simplistic but no less compelling (at least for those who recognize homo economicus as an ideal type, not a descriptively accurate model of human behavior).

The basic idea is that at least some addictive, mind-altering substances may merit an exception to the general rule that a liberal society should not interfere in the private consumption decisions of its citizens. Mark Kleiman, a drug policy scholar and professor at UCLA, eloquently makes the case in his 1992 book *Against Excess.* The distinguishing characteristics are a combination of factors such as in the following examples: Drugs are intoxicating, so consumption decisions are often made "under the influence"; for some, drugs cessation is physically painful; drugs offer immediate pleasures and the possibility, but not guarantee, of delayed pain; drug initiation occurs primarily among minors; social influences play a prominent role in initiation decisions. That skepticism of government regulations is healthy for a liberal democracy does not imply that prohibiting a drug is necessarily a bad idea. Liberal democracies tolerate other paternalistic infringements on freedom of behavior (e.g., a minimum wage, motorcycle helmet laws, and prohibitions against swimming where there are dangerous rip tides).

Furthermore, few want minors to have ready access to drugs, but legalizing use by adults inevitably makes a drug readily available to minors because every adult is a potential supplier, whether consciously (e.g., adults buying alcohol for minors) or unconsciously (e.g., minors stealing cigarettes from adults). Legalizers sometimes deny this connection, asserting that cocaine is more readily available to minors than alcohol is, but those assertions are contradicted by minors' self-reports (e.g., in the Monitoring the Future surveys). The moral arguments for or against prohibition are in one sense unassailable. Individuals are entitled to their separate values. But at the same time those values are not likely to be persuasive to people who do not hold them.

For consequentialists, opinions about legalization tend to depend on two factors: (1) how people trade off or value the problems associated with drug use and those associated with prohibition and black markets and (2) on predictions about how legalization would affect those outcomes. Prohibiting a drug will generally reduce but not eliminate its use. The use that persists despite prohibition supports a black market, which generates problems of its own. Indeed, the social cost per gram or per ounce consumed will typically be greater than would be the case if the drug were legally available. So prohibition typically reduces use but increases harm per unit of use.

Those who favor legalization tend to believe that a drug's legal status has little impact on its use. They also tend to be very mindful of the problems associated with black markets (stereotyped as drug dealers shooting people in battles over competing

territories), drug enforcement (e.g., racially biased enforcement tactics), and prohibition's increasing the damage per episode of use (e.g., restricting needle availability, increasing spread of HIV by needle sharing). Those who favor prohibition tend to believe that prohibition substantially suppresses use (tobacco and alcohol are used far more than cocaine or heroin) and that many problems stem directly from drug use (e.g., the damage addiction can do to familial relations) not primarily from the drug's illegal status. To them, legalization is tantamount to making a bad situation worse. It might eliminate the black market and associated crime, but if legalization led to a tenfold increase in the number of addicts, the country could still be worse off.

Unfortunately, the public debate about the consequences of legalization is clouded with specious arguments. For example, prohibitionists argue that drugs should be illegal because they are associated with so much crime. Indeed, the majority of arrestees in many U.S. cities test positive for illegal drugs; association does not imply causality, but a reasonable guess is that something on the order of one-fourth of crime in the United States is caused by illegal drugs. Legalizers counter that most of the drug-related crime is attributable to the illegality, not the drugs per se. Only about one-sixth of drug-related crime is psychopharmacological in nature (i.e., driven directly by intoxication or withdrawal). Conflicts between market participants turn violent in part because they cannot resort to the court system to resolve disputes, and one reason addicts commit robberies is to get money to buy drugs that would cost far less if they were legal. Ironically, alcohol is one of the most violence-promoting substances per se, and it is legal.

To give an example from the other side, legalizers cite statistics showing that illegal drugs such as cocaine and heroin kill only thousands of people per year, whereas alcohol and cigarettes kill hundreds of thousands. What they neglect to point out is that far more people use cigarettes and alcohol, so the death statistics per user are not so different. Furthermore, the death statistics for illicit drugs are restricted to acute effects (e.g., overdose deaths), whereas the cigarette and alcohol figures include indirect effects (e.g., deaths caused by intoxicated drivers) and delayed or chronic effects (e.g., from lung cancer). Focusing on overdose deaths would make cigarettes seem safe, whereas the expansive definition suggests that they kill more people than all other drugs combined, including alcohol.

Both sides lend a patina of scientific rigor to their arguments by citing trends in data, but the divergent trends of different indicators makes it easy to tell statistical lies. An advocate of prohibition might point out that the number of drug users fell dramatically during the 1980s when enforcement expanded rapidly. A legalizer could counter that emergency room mentions of drug use rose as fast as prevalence fell. What is lost in such bickering is the observation that the legal status of the major drugs has been stable in the United States for many decades. Looking at contemporary trends might indicate the wisdom of a more or less stringent prohibition, but there is no direct experience with legal cocaine, heroin, marijuana, or methamphetamines in recent U.S. history. Many seek to draw lessons from other times (e.g., when cocaine was legal in the United States in the late nineteenth century) or places (e.g., Europe), but casual comparisons can be misleading and careful study of those analogies does not give definitive guidance (MacCoun & Reuter, 2001).

Even anecdotal evidence can be spun in different ways. Occasionally, there are accounts of a mother selling her baby for crack. Some argue this kind of action proves drugs should be legalized. If they were cheap enough, addicts would not have to resort to such extreme measures. Others counter that the fundamental problem is that the drug is so powerful that it becomes more important to a mother than her own child; therefore, everyone should be protected in whatever ways possible from exposure to such temptations that can erode basic human values and worth.

The next important observation is that different drugs are different, and it may well make sense to prohibit some but not others because they have different properties (e.g., some drugs can trigger violent outbursts [PCP]; others tend to sedate [heroin]). It is by no means the case, however, that one can unambiguously rank substances from the most to the least dangerous because a substance can be very threatening in one respect but not in others. Cigarettes are highly addictive, but they are not intoxicating. Heroin can be deadly

	Caffeine	Tobacco	Alcohol	Marijuana	Heroin	Cocaine
Acute health risk	None	None	High	Minimal	High	Moderately High
Chronic health risk	None	Huge	High	Some	Minimal	Some
Use affects health of others	No	Yes	Fetuses	Possibly	No*	Fetuses
Problems caused by withdrawal	Minimal	Unpleasant	Physical risk	Minimal	Physical risk	Extremely unpleasant
Intoxication leads to accidents	No	No	Yes	Some	Moderate	Unclear
Intoxication leads to violence	No	No	Yes	No	No	Some
Likelihood of addiction given use (as observed in the U.S. in last 30 years)	Minimal	High	Moderate	Moderate	High	High
Addiction disruptive to daily functioning	No	No	Yes	Somewhat	Yes	Yes

*Injection drug use can spread blood-borne diseases (BBDs), including HIV/AIDS and hepatitis, but it is injecting with shared equipment, not the heroin use per se, that is the proximate source of the spread of BBDs.

Table 1. Substances and their risks. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

(overdose deaths are not uncommon) but in and of itself creates almost no chronic health damage. Heroin addicts are usually in poor health because they are poor, spend money on heroin rather than on food or shelter, and inject with dirty needles, but the heroin per se does not degrade organs the way alcohol destroys the liver or smoking causes emphysema. Table 1 illustrates the concept.

The table divides the substances by legal status. The legalization question asks whether any substances on one side of the line should be moved to the other. It does not address changes in laws, programs, or policies that do not move a substance across the line. It might or might not be a good idea to repeal mandatory minimum sentences, cut the number of drug arrests in half, expand treatment and prevention programs, approve marijuana for medical use, eliminate profiling as an enforcement tactic, reduce the military's role in drug control, and repeal drug-related civil forfeiture statutes. Doing so would blunt many of the criticisms of prohibition, but it would not constitute legalization. Conversely, one could raise the legal smoking age, require people to pass a drinker's test to get an alcohol consumption license, or ban smoking from all public spaces, but none of those would extend prohibition to a new substance.

There is no constituency for prohibiting caffeine, and prohibition of alcohol is perceived to have failed so badly in the last century that there is little interest for trying it again. There is some discussion of banning tobacco use, but such proposals are probably political non-starters.

The more seriously debated proposals would legalize one or more of the substances prohibited as of 2008. For discussion purposes, it is convenient to differentiate three groups of substances: (1) cocaine, heroin, and methamphetamines, (2) marijuana, and (3) all other illicit substances.

Cocaine, heroin, and methamphetamine are not similar pharmacologically, but they have key commonalities. They are expensive, are subject to stringent enforcement, can dominate the life of an abuser, and have large, established black markets. These are the substances whose use can most confidently be predicted to rise substantially and to be problematic if they were legalized. These substances are very simple to produce, but sell for many times their weight in gold because they are prohibited and subject to severe sanctions. They are also the source of most of the corruption,

violence, and disorder associated with drug markets, so legalization would bring many benefits. Most observers, though, believe this would be an example of making a bad situation worse. At a minimum, legalizing these substances is a high stakes gamble that is only partially reversible. There are other, safer alternatives to exhaust first (e.g., mending rather than ending prohibition) and more information that should be gathered about how legalization would affect use before seriously contemplating such a radical change.

Marijuana presents quite a different situation. Prohibition makes marijuana more expensive than it otherwise would be, but a daily habit is no more expensive than a two-pack a day cigarette habit. Likewise, daily marijuana use is not a recipe for enhancing performance, but it does not preclude most daily functions (e.g., personal hygiene, holding down a job). So a tenfold increase in use is a less likely outcome of legalizing marijuana than for cocaine, and even if it did happen, that outcome would be less catastrophic. However, the benefits of legalizing marijuana are also far smaller than the benefits of legalizing cocaine, heroin, and methamphetamines because marijuana markets are less violent and marijuana users generally do not resort to crime to support their habit. Likewise, marijuana offenders account for only about 10 percent of those in prison for drug law violations. There is no consensus about whether legalizing marijuana is wise. Some say yes. Many say no. What is clear, though, is that the risks, uncertainties, and potential benefits are all much smaller when considering legalizing marijuana than when considering legalizing cocaine, heroin, and methamphetamines.

The last category is diverse, so general statements are difficult. It includes drugs that can be used as a weapon in sexual assault (e.g., GHB) and drugs used not for their mind or mood altering properties but to enhance athletic performance (e.g., anabolic steroids). Two general observations are possible, however. First, prohibitions are relatively more effective and relatively less costly when preventing the spread of substances that are not commonly used than they are at reducing the use of an established drug. Second, by definition, there is more to lose in terms of increased availability and use when altering the status of drugs that are now rare. By those principles, it would be easier to make a case for legalizing XTC (Ecstasy) or LSD, for example, than for PCP, but they are not frequently the focus of legalization proposals, which typically address just marijuana or all drugs collectively.

See also **Cocaine; Heroin; Legal Regulation of Drugs and Alcohol; Legalization vs. Prohibition of Drugs: Historical Perspective; Marijuana (Cannabis).**

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LIMBIC SYSTEM. The limbic system is a group of brain structures organized into a functional unit that is important in the expression of emotion and mood states. The term *limbic lobe* and associated terminology can be traced to the French neuroanatomist Paul Broca (1824–1880), who used it first to describe the forebrain structures that encircle the brain stem. The *limbic system* is a broader classification, composed of brain structures that form an integrated circuit surrounding the thalamus—an important relay station between higher brain centers and the hind brain and spinal cord.

The limbic system is thought to be important in emotional behaviors. This was hypothesized on the basis of neuropathological investigations of the brains of individuals displaying bizarre emotional disturbances. These initial clinical observations were followed by animal studies, in which the loss of these structures produced significant changes in emotional responsiveness. As research techniques and methodologies were refined, it became clear that limbic structures had an important and complex role in the expression of behavior. It is now believed that these structures are involved in a number of significant behavioral processes. In particular, the limbic system and related structures are thought to be important in the expression of emotion related to euphoria and feelings of well-being. For these reasons, the limbic system may have an important role in drug abuse.

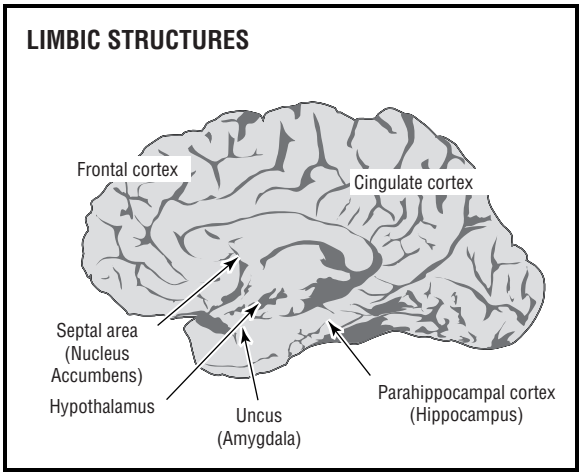

Figure 1. The limbic system—composed of structures generally located between the brain stem and higher cortical structures. Some of these components are labeled in the sagittal section of the brain. The structures in parentheses lie behind the structures listed above them. The hypothalamus, hippocampus, septal nuclei, nucleus accumbens, amygdala, cingulate cortex, and frontal cortex are components of the limbic system that may have an important role in drug abuse. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

LIMBIC SYSTEM COMPONENTS

The limbic system that surrounds the thalamus provides an interface between the midbrain and higher cortical structures. The general structure and components of the limbic system are shown in Figure 1. These include the amygdala, the nucleus accumbens, the olfactory tubercle, the septal nuclei, the hippocampus, the hypothalamus, the cingulate cortex, and the frontal cortex. As can be seen in the figure, these structures are positioned between the brain's major relay station—the thalamus—and higher cortical structures. The separate components of the limbic system are interconnected such that activity initiated in one structure affects other components. One of the hypotheses about the basis of emotion speculated that reverberating neuronal activity in this system was responsible for affective behaviors. Initial animal studies using either direct electrical stimulation or lesions (loss) of various components of the limbic system substantiated the important role of this system in behavior.

THE ROLE OF THE LIMBIC SYSTEM IN BEHAVIOR

Electrical stimulation or the destruction (lesions) of components of the limbic system alter behavioral processes. Lesions of the hippocampus disrupt memory processes, whereas lesions or stimulation of the amygdala affect emotional behavior and feeding in a manner similar to manipulations of the medial and lateral hypothalamus. Stimulation of the lateral hypothalamus produces aggressive responses, whereas lesions of this area produce a placid behavioral profile. In contrast, lesions of the medial hypothalamus produce a highly excitable and aggressive pattern of behavior, whereas lesions of the amygdala result in placid and nonaggressive behavior. Early studies found that lesions of the lateral hypothalamus can decrease feeding, whereas lesions of the ventromedial region produce excessive levels of feeding resulting in obesity. Recent experimental studies have demonstrated the complex nature of the involvement of hypothalamic cells in feeding and drinking; however, like most complex behaviors, the mechanisms that control hunger and satiety are not simply located in a single brain center.

Some structures of the limbic system are important in reinforcement processes. The term *reinforcement* applies to processes perceived as rewarding or good, which therefore are repeated, such as electrical self-stimulation. For example, animals will repeatedly emit a response that leads to the delivery of brief electrical stimulation of small electrodes that are implanted in selected brain structures. Humans will also choose to stimulate many of these same brain regions and report positive feelings of well-being and euphoria. The limbic system sites that produce these effects in animals include the lateral hypothalamus, nucleus accumbens, frontal cortex, cingulate cortex, and the brain-stem nuclei believed to be part of the limbic system—these include the substantia nigra and ventral tegmental area, which both contain dopamine neurons that send inputs to many limbic-system components. Measures of brain-glucose metabolism, which directly reflect brain-cell activity, have been used to determine the involvement of specific brain regions in animals electrically self-stimulating three of these brain regions. The stimulation of each of these regions produced significant activation of several limbic-system structures that included the nucleus accumbens, amygdala, hippocampus, and the frontal and cingulate cortices. This area of investigation has led neuroscientists to propose that there are brain circuits

dedicated to the behavioral processes related to reinforcement. Drugs of abuse likely produce their positive effects through the activation of these brain circuits.

THE ROLE OF THE LIMBIC SYSTEM IN DRUG ABUSE

A large number of experiments have focused on identifying the brain circuits that mediate the reinforcing effects of abused drugs, because the reinforcing effects are responsible for drug abuse. These experiments have included the use of drug self-administration techniques and sophisticated neurochemical procedures to measure the involvement of specific neurotransmitter systems. As of 2008, evidence indicates that limbic structures and brain cells that project to limbic structures play an important role in these processes. It is clear that dopamine-containing neurons that project from the ventral tegmental area to the nucleus accumbens have a critical role in the reinforcing actions of cocaine and amphetamine. Removal of these inputs with toxic agents that selectively destroy dopamine-releasing brain cells disrupts intravenous self-administration of these drugs. Additional evidence of the importance of this region in drug abuse comes from glucoseutilization studies. The levels of glucose metabolism are significantly elevated in a number of limbic structures in animals self-administering cocaine intravenously. Other experiments have directly shown dopamine levels in the nucleus accumbens to be increased in animals intravenously self-administering cocaine. Collectively, these data imply an important role for the limbic system in general and specifically for dopamine neurons in the limbic system tied to the brain processes involved in stimulant abuse.

The brain circuits involved in opiate reinforcement appear to be very similar to those mediating cocaine self-administration. Limbic structures are clearly implicated in opiate reinforcement, but a central role for dopamine is less obvious. Significant changes in the utilization of some chemicals (neurotransmitters) involved in transmission between brain cells have been shown in the nucleus accumbens, amygdala, and the frontal and cingulate cortices of animals intravenously self-administering morphine. However, loss of dopaminergic inputs to the nucleus accumbens does not affect drug intake, whereas a similar loss of serotonergic inputs does. Similarly, nucleus-accumbens dopamine does not appear to be elevated in animals self-administering heroin as it is in animals self-administering cocaine. However, evidence does indicate an important role for limbic structures and chemicals used to communicate between cells of the limbic system in opiate reinforcement. Limbic structures also appear to be important for ethanol (drinking alcohol) reinforcement. The levels of dopamine appear to be elevated in the nucleus accumbens of rats orally self-administering alcohol. Injections of drugs that antagonize dopamine directly into the nucleus accumbens decrease alcohol self-administration, whereas drugs that enhance dopamine action increase alcohol intake. In addition, animals will self-administer alcohol directly into the ventral tegmental area—an area that contains the cell bodies for the dopamine cells that send inputs to the nucleus accumbens. These data collectively indicate that the nucleus accumbens and dopamine-releasing inputs to the nucleus accumbens are important to alcohol reinforcement.

CONCLUSION

The limbic system plays an important role in behavior. These brain structures appear to be central to the processes that mediate the reinforcing effects of electrical-brain stimulation and of several highly abused drugs. The nucleus accumbens appears to be a structure central to the reinforcing properties of cocaine and amphetamine, but it appears less important to opiate and alcohol reinforcement. A more exact definition of specific neurochemicals and brain-cell pathways in the limbic system that are involved in drug abuse will become clearer as new methodologies are developed.

See also **Neuron; Neurotransmission.**

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LYSERGIC ACID DIETHYLAMIDE (LSD) AND PSYCHEDELICS.

LSD is the abbreviation for lysergic acid diethylamide. It is the most potent member of a group of hallucinogenic substances called the indole-type hallucinogens. These drugs have structural similarities to another indole, the neurotransmitter serotonin.

HISTORY

LSD was originally synthesized at the Sandoz Pharmaceutical Company in Switzerland as part of a long project begun in the 1930s. The aim was to develop useful medications that were derived from ergot, a fungus (*Claviceps purpurea*) that infects such grasses as rye. Some of these compounds were found to be useful in medicine—such as methysergide, for the treatment of migraine headaches, and ergotamine, which is widely used in obstetrics to induce contractions of the uterus and stop bleeding after the delivery of a baby. These medications do not have hallucinogenic properties.

The chemist in charge of this drug development project was Albert Hofmann. In 1943, he synthesized a compound he called LSD-25 because it was the twenty-fifth compound made in this series of ergot derivatives. He accidentally ingested some of it and within forty minutes had the first LSD "trip." He told his colleagues he was not feeling quite right and got on his bicycle to go home. Later, he carefully described the vividly clear flood of perceptions that are characteristic of the "mind manifesting" or psychedelic drug. This, then, was a complete surprise. Thereafter, the drug and various substitutions of different atoms on the basic molecule were extensively tested for medical uses in the late 1940s and in the 1950s. No specific medical use of LSD or its psychedelic variants has been found.

Because of its potency and the extensive reports of laboratory studies in animals and in the clinic, LSD has become the prototypical hallucinogen, or psychedelic drug. It also became the emblem of a social movement—which, in fact, was a confluence of various movements that had begun in the early 1960s; they peaked in the late 1960s. By 1973, the "acid culture" had subsided into a small but still active subculture of various psychedelic drug devotees seeking meaning and profound insights. The feeling of a "great discovery" about such drugs and the human mind had occurred as early as the nineteenth century; artists and writers, such as Baudelaire and Rimbaud in Paris, had discovered hashish and the altered, somewhat dreamy, states of consciousness and euphoria produced by this potent form of marijuana—the active ingredient of which is tetrahydrocannabinol (THC). For a period, they became absorbed with hashish and wrote about its alluring effects. The drug scene evoked the promise that the human mind must contain remarkable powers. Toward the beginning of the twentieth century, mescaline, the active hallucinogenic compound in the peyote cactus, similarly was tried by a few explorers in medicine and in the arts. In New York City, during the early part of World War I, many influential people and intellectuals took either peyote "buttons" (the dried tops of the peyote cactus) or mescaline (the synthesized active ingredient of the buttons) and called it a "dry drunk." Similarly, after World War II, LSD caused a flurry of excitement among some professionals, and its medical value was tested in psychiatric patients. Writers such as Aldous Huxley wrote exciting books about the effects of mescaline and, later, LSD—yet there was still no widely popular movement until 1960.

Then Timothy Leary, a young psychology instructor at Harvard, explored the Mexican or "magic" mushroom, *Psilocybe mexicana*, and its active ingredient, psilocybin—and later LSD—claiming criminals became loving and peaceful and others more creative. He popularized this on campus and, when he was not reappointed to the faculty, proclaimed himself to be a martyr to his

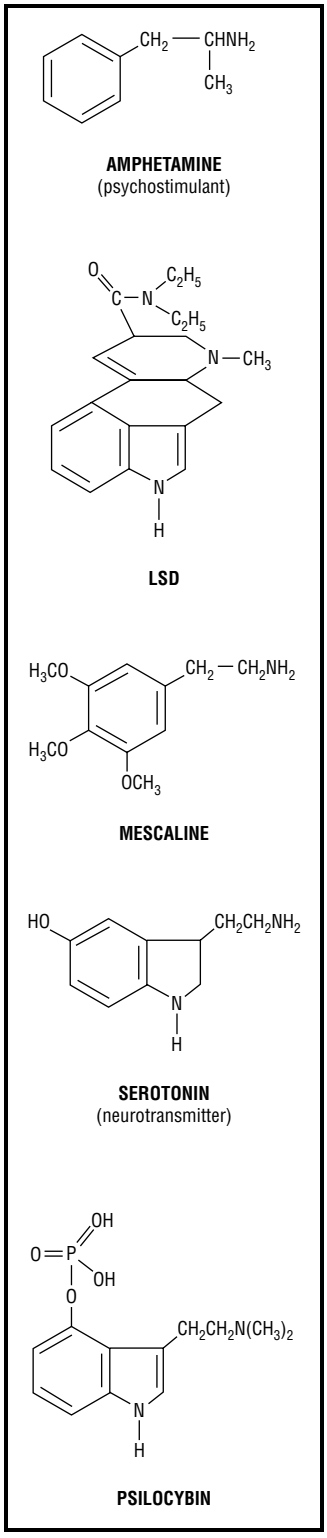

Figure 1. Chemical structures of amphetamine, LSD, mescaline, serotonin, and psilocybin. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

cause. Between 1960 and 1966, the media repeatedly "discovered" LSD—in effect, advertising it. As publicity increased, subcultures experimenting with mushrooms and LSD grew up in the East and West Coast cities. Musicians, rock music, the hippie lifestyle, "flower children," and many in the various protest movements against the Establishment and the Vietnam War were loosely joined to Leary's attempt to lead affluent and middle-class youth. Well-publicized festivals celebrated LSD and marijuana, such as the Summer of Love in the Haight-Ashbury section of San Francisco. Leary's challenge was for youth to "turn on, tune in and drop out" with acid. As more and more youth were curious to try experiences their parents had never dreamed of, rebellion led not only to acid experiments but to extensive polydrug abuse—the extensive use of marijuana and various street substances. Either LSD or some variant and even heroin were tried. In addition, the search for new drugs with different and improved characteristics (more or less euphoria, hallucinogenic activity, or stimulant properties), literally hundreds of so-called designer drugs were synthesized (DOM, MDMA, DMT, etc.). Because any drug can have bad effects, the unsupervised use of all of these compounds led to frequent "bad trips" (which fundamentally were panic reactions) that brought people to emergency rooms. This generated widespread concern that all American youth (and, later, those in Europe) would become dreamy and "way-out acid heads." In 1966, the Sandoz Laboratories ceased distribution of the drug because of the often-exaggerated bad reactions and the public concern. As the claims for enduring LSD insights proved transient, research with LSD in humans essentially stopped.

Thus, one of the ways people use the effects of drugs that seem to enhance the clarity of mentation (mental activity) and perception (while not producing confusion, dreamy-euphoria, or oversedation) is to become absorbed in periods of intense exploration with a few others "in the know." Those with such inside information form a kind of cult and then advertise, but they eventually see some bad effects (the wrong people taking the drug in the wrong circumstance with unfortunate consequences) and sooner or later see little real use for the drugs. The minor or major epidemics then die down, only to recur as later generations rediscover the compounds.

Dr. Timothy Leary, center, in custody, being led to U.S. Customs House at La Guardia Airport, 1966. © BETTMANN/CORBIS.

EFFECTS

LSD is one of the most potent hallucinogens known; one-billionth of a gram of LSD per gram of brain produces profound mental changes. Although subjective effects occur in some individuals after doses as low as 50 micrograms, typical street doses range from 10 to 300 micrograms—street dosages vary widely. Misrepresentation also frequently occurs; someone will try to purchase synthetic tetrahydrocannabinol (THC), the active ingredient of marijuana, and receive LSD. Thus, the intake of LSD can be accidental as well as intentional, and the lack of quality control in illicit supplies is a hazard. Because of its high potency, LSD can be applied to paper blotters or the backs of postage stamps from which it is dissolved for consumption. Unsubstantiated reports of LSD added to stick-on tattoos for young children have caused alarm, even though absorption through skin would be far too slow to deliver enough drug to the brain to produce and sustain a trip.

The absorption of LSD from the gastrointestinal tract and other mucous membranes occurs rapidly, with drug diffusion to all tissues, including brain. The onset of psychological and behavioral effects occurs approximately 30 minutes after oral administration, peaks in the next 2 to 4 hours, depending on the dose, with gradual return to normal by 10 to 12 hours. The first 4 hours after a 200-microgram dose are called a trip. In the next 4 to 8 hours, when over half the drug has left the brain, the "TV show in the head" has stopped. At this point subjects think the drug is no longer active, but later they recognize that they, in fact, had paranoid thoughts and "ideas

of reference" in the last 4 to 8 hours of the trip. This simply means that there is the feeling of being at the center of things, being hyperalert, and having a conviction that everything going on refers to oneself. This is a regular but little-publicized aftereffect, which finally dissipates 10 to 12 hours after the dose.

From 12 to 24 hours after the trip, there may be some slight letdown or feeling of fatigue—as if one had been on a long, steep roller coaster ride. After these intense and even frightening moments, the ordinary world might for a time seem drab. There is no craving to take more LSD to relieve this boredom; one trip usually produces satiation for a time, although some may want to repeat the experience. Memory for the events during the trip is quite clear. Those who revisit the experience sooner or later decide they have learned what they can and go on with the practical, daily affairs of living. In one experiment on creativity, subjects received either LSD or the stimulant amphetamine during a period of pleasant surroundings and music. The only difference between the two groups six months later was a slight tendency for those who had received LSD to buy more recordings! So the promise of lasting insight or creativity was not kept.

Drugs that make one feel different—alcohol being typical—can signal a "holiday from daily reality." The way the effects of such drugs are interpreted is critical. Beer at the Super Bowl means "loudly letting go" and champagne at the White House means a time for graceful speech and feelings. Thus personal and social expectations (called *set*—or how one is set to go) and the surroundings (called *setting*) have much to do with the ultimate effects of drugs. This is distinctively and especially the case with psychedelics. Thus when the chemist Albert Hofmann first ingested the active ingredient of the Mexican mushroom psilocybin, the perceptions capturing his attention were related to Aztec symbols and art! For some, therefore, the trip may simply be funny and odd—for others it will have special meanings. Set and setting partially determine the character of such trips.

Fundamentally, LSD produces a heightened clarity and awareness of sensory signals—of sights, sounds, touch, lights, and colors. Similarly there is special significance given to thoughts, memories, or verbal interchanges. For example, gestures or inflections of speech or many cues that are normally in the background are felt to be more important than what is being said or usually meant—and in looking at a picture, the central figures may take on a life of their own, the small background details that are normally ignored emerging, capturing attention.

While awareness is strikingly increased, control over what is being attended to is weakened. For all these reasons, unstable surroundings or confused motives at the time of drug ingestion may lead to a less-controlled trip or even a panic-generating trip. Many are aware that the trip is not quite real and fundamentally feel as if they are "spectators" of what they are so intensely experiencing. Many rely on guides, a group, or the rhythm of music to carry them through this period of altered perceptions in which control is diminished. Thus, personal intent and reliable surroundings are major factors affecting the different kinds of experiences that people will have.

While every trip has an individual characteristic, there are regularities in the trips. This has been called a "march of effects" following drug ingestion. Thus, observers note, the first sign of feeling different is like "butterflies in the stomach" or a slight nausea and feeling of "whoops, here we go" as if on a roller coaster. Parts of the body simultaneously feel strange or different. At about the same time (30–40 minutes after drug ingestion), the cheeks are slightly flushed and pupil size begins to increase, maximizing within an hour or two. These changes are due to the effects of LSD on the sympathetic and parasympathetic nervous systems. The pupils react normally but are enlarged. After 4 hours they slowly begin to return to normal size, which finally is achieved at 10 to 12 hours after taking LSD. At the beginning of the trip, all soon note that what is at the periphery of their vision suddenly seems as clear as what is normally at the center of vision. Over the next 90 minutes, there is a feeling that tension is welling up. Laughing or crying will relieve the tension. Often subjects say they are laughing because of what they see or crying because of their feelings. But this is simply based on a need to relieve the fluctuating rise of tension. The trip moves on into the second and third hours when perceptual fluctuations and intensities are mainly noted. People also report perceiving several feelings simultaneously. A

common observation is, "I don't know if I'm anxious, thrilled, or terrified." Just as perceptions are in flux, so are feelings, and these feelings and emotions may capture center stage in the second and third hours. Throughout the trip, people feel as if they are on the brink of an exhilarating but also dangerous experience. This intensity dies down about 4 hours after the usual dosage. If very large doses of LSD (500–1,000 micrograms) are taken, there is less capacity to be a spectator and far more intense self-absorption and fear. Some call this "dying of the ego" and relate the experience to mystical versions of death and rebirth.

Because the familiar seems novel and is seen in a different way, specialists in perception have been interested in what is called the "breakdown of constancies" that occurs with the drug. Normally we correct for what the retina sees by putting the world into order. We usually suppress the nonessential and focus on what we need to do to get about during the day. Just as with a camera, the retina sees the hand placed 6 to 8 inches in front of the eye as large. But the brain corrects for it and keeps size constant. Under LSD, corrections for constancy do not seem to happen. Many sensations that are normally dampened can thus have free play under the drug and the world will seem far less regular than it does in daily life.

One of the aftereffects in some—clearly not all—people is called "flashbacks." Days, months, or years after tripping, with no particular trigger or with an intense sensation, there may be a sudden few minutes in which subjects feel like they are back under the drug. They also may see flashing lights and other optical illusions. These flashbacks may be very disturbing. Flashbacks can occur after only a single drug experience and unpredictably. There has been no explanation as to why or how flashbacks occur. Scientists cannot predict (by observing a trip) if flashbacks will later occur or who is vulnerable. While these aftereffects are upsetting to some, most people do not experience them or those that do are not bothered. Others simply observe that their dreams may be more intense for a time after the drug experiences. One scientist noted that riding on a train to work, he was distracted from focusing on his newspaper for several months by the telephone poles whizzing by. These were normally at the periphery of his attention as he was reading, but after LSD, he could no longer suppress this irrelevant detail. There were more reports of such phenomena after publicity about them; given the millions of trips with LSD, these aftereffects are certainly infrequent but not rare.

Perhaps the most alarming bad effects of the drug have been the panic states occurring during a trip. Native Americans note that if one is in conflict, the effects of mescaline during religious ceremonies are unpleasant and can evoke terror. They then pray with the panicked person and "talk him down." One cannot predict whether a panic experience will occur. "One good trip does not predict a second one" is the general wisdom concerning this risk. Higher doses lead to less control and more intense effects, but panic states can occur at doses as low as 75 to 100 micrograms. For those who might be at risk for other mental disorders, hallucinogenic experiences may often destabilize them and precipitate some form of mental illness. For others, the experience may lead to a subsequent absorption with the unreal ("dropping out"), rather than coping with the challenges that the tasks of the ordinary world present. Occasional suicides or rare impulsive acting out of odd ideas arising during a trip have led some to loss of control and tragedy.

For most, the experiences have few negative or positive aftereffects. Although it has often been suspected, no permanent change to the cells of the brain (brain damage) has ever been scientifically established. There is no generally accepted evidence that the drug produces chromosomal abnormalities or damage to a developing fetus (although no nonprescription drugs during pregnancy is the only safe rule to follow). The bad effects of a period of diminished control are unpredictable, and in that fact lies the real risk. Thus, it is the intensity of the experience and how well or poorly it can be managed, the unpredictable flashbacks, and how this "TV show in the head" or this "waking dream" gets woven into one's subsequent life that are at issue when hazards are considered.

TOLERANCE

One striking feature of LSD, mescaline, and related psychedelic drugs is tolerance, which is a loss of typical drug effects after repeated doses. In

brief, with daily doses the duration and intensity of effects rapidly diminish to the point where no subjective effects are perceived. After 200 micrograms per day of LSD, there is simply no detectable drug effect on the third or fourth day. After three or four days without LSD, the full initial effects can be triggered by the same dose that has been "tolerated." Thus tolerance develops and dissipates rapidly. When subjects are tolerant to LSD, the usual dose of mescaline required for a trip is also no longer effective. This is called cross-tolerance. It is readily seen with similar dosage schedules of psilocybin, LSD, and mescaline. There is no cross-tolerance with the nonhallucinogenic stimulant drug amphetamine. Thus, there must be some common mechanism of action among the psychedelic drugs beyond their structure and similar array of mental effects.

Tolerance is seen both in humans and laboratory animals. The lack of pupil enlargement is a common sign of tolerance. In animals, some drug effects show tolerance and some do not. For example, a heightened sensitivity of rats to mild electric shock persists after daily doses and does not show tolerance. Such persisting drug effects during periods of tolerance have not been studied in humans. How and why a psychedelic drug loses and regains its potency in this fashion is not yet understood, but there is no withdrawal discomfort after stopping a psychedelic drug when it has been taken over several days. This differs from the classic effects described for opioid drugs, where an uncomfortable withdrawal with drug cessation requires more drug for relief. Such physical drug withdrawal phenomena are not found with psychedelics.

LSD AND SEROTONIN

LSD is known to affect many places in the brain where the body's neurotransmitter serotonin naturally has actions and effects, and the biochemical effects of LSD in the brain are mostly linked to those sites related to serotonin. LSD acts as a kind of impostor at receptors that recognize serotonin. LSD is like serotonin but different. Thus with LSD, the receptor signals other parts of the brain that there is too much serotonin, and these parts of the brain respond by tuning down cells that make serotonin. Yet, in fact, the chief effect of LSD is to cause *less* serotonin to be released in the neighborhood of the receptor—rather than too much, there is too little. This is one example of how LSD miscues the systems governing the flow of information between various brain neurons. In fact, overloading the brain with serotonin can reduce the LSD effect, and diminishing brain supplies of serotonin will increase LSD effects. Yet serotonin itself does not cause the scrambled perceptions that LSD does. How this miscue by LSD leads to the vivid effects is still unknown.

LSD, other indole-type psychedelics, and many hallucinogens related to mescaline (but surprisingly not mescaline itself) are known to act especially at a subtype of the serotonin receptor called the $5HT_2$ receptor. In laboratory animals, daily doses of LSD or psilocybin lead to fewer of these receptors, an effect that would be expected to produce tolerance; however, with 3 or 4 days off the drug, the number of $5HT_2$ receptors returns to normal. Both LSD and mescaline act at certain brain neurons, such as the locus coeruleus, and make it more responsive to inputs from the environment—such as a pinch. Researchers speak of such effects as lowering the gates to sensory input. We know the ways by which LSD affects certain brain systems but still far less than we need to know to explain the full panoply of effects.

Although many of the psychedelic drugs are known to interact with serotonergic $5HT_2$ receptors, and this interaction appears to be of critical importance in producing their hallucinogenic effects, the hallucinogenic drugs can bind to a subtype of serotonin receptors that is located on serotonin nerve-cell bodies and on their terminals (which release serotonin that goes to the adjacent nerves with $5HT_2$ receptors). Interactions with these various receptors can lead to changes in the firing rate of such cells. The designer drugs MDMA and MDA cause the release of both dopamine and serotonin, effects that might contribute to their psychostimulant properties. The differential interactions of the various hallucinogens with multiple sites and systems may underlie the qualitative differences in the experience they produce.

See also **Cults and Drug Use; Hallucinogenic Plants; Monitoring the Future; Plants, Drugs From.**

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Third Edition


HENRY R. KRANZLER & PAMELA KORSMEYER

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MANDATORY SENTENCING. Mandatory sentencing laws provide that people convicted of particular crimes receive particular sentences. Examples include laws specifying that people convicted of selling heroin or cocaine within 1,000 yards of a school receive at least a three-year prison term or that people convicted of selling more than four ounces of heroin or cocaine receive at least a five-year prison term. The latter are referred to as mandatory minimum sentences. Some mandatory sentencing laws require life sentences. A Michigan law, for example, which the U.S. Supreme Court upheld against a claim that mandatory life sentences constitute "cruel and unusual punishment" in violation of the Eighth Amendment to the U.S. Constitution, required life sentences without possibility of parole for people convicted of possessing more than 650 grams of cocaine (*Harmelin v. Michigan*, 49 Cr.L. 2350 [6/27/91]). An Alabama law required life sentences for people who, having previously been twice convicted of felonies, are convicted of a third felony. Laws like Alabama's are sometimes called *habitual offender* or *predicate felony* laws.

ENACTMENT OF MANDATORY SENTENCING LAWS

An unprecedented number of mandatory sentencing laws were enacted during the 1970s and 1980s. Most involve drugs, firearms, or both. New York, under Governor Nelson Rockefeller, was the first state to enact mandatory sentences. Known as the Rockefeller drug laws, these acts imposed mandatory 15-year and life sentences for certain drug offenses. These harsh laws set off a chain reaction. Between 1978 and 1981, forty-nine states enacted mandatory sentencing laws. Every state and the federal government enacted mandatory sentencing laws during the 1980s. In 2007, over one hundred separate mandatory minimum penalty provisions were contained in federal criminal statutes.

Apart from specific offenses that carry mandatory sentences, state and federal sentencing guidelines mandated that judges impose minimum sentences based on the crime committed, aggravating factors, and the criminal history of the defendant. These guidelines increased punishment for criminal offenses and limited judicial discretion in sentencing by identifying the punishment required upon conviction for a particular offense. Many of these statutes eliminated or greatly restricted parole for prison inmates. Congress passed the Sentencing Reform Act of 1984 (SRA), which eliminated parole for federal prisoners and reduced the amount of time off granted for good behavior. The SRA also established the U.S. Sentencing Guidelines Commission and directed it to create a new sentencing system. In 1987, the commission's guidelines became effective.

The popularity of sentencing guidelines in the United States marked a rejection of indeterminate sentencing. Under indeterminate sentencing, judges set maximum lengths of prison sentences, and sometime minimums, but parole boards decide when a prisoner will be released. In contrast, the Federal Sentencing Guidelines shift the focus in sentencing from the offender to the offense. The guidelines categorize offenses and identify the sentence required upon

conviction. Judges are allowed to increase or decrease sentences, which are called *departures*, only if they have good reasons and cite these reasons into the trial record. *Upward departures* are easy to achieve, as judges are allowed to consider all relevant conduct. This conduct can include the circumstances surrounding the crime, offenses that were committed at the same time as the charged offense but were not charged, prior convictions, and acts for which the defendant was previously tried but acquitted. Federal judges have a more difficult time decreasing a sentence. A *downward departure* is acceptable if the defendant accepts responsibility for the crime or committed the crime to avoid a more serious offense. Prosecutors often successfully challenge decreases in sentences on appeal.

Mandatory sentencing laws have long been controversial. The American Law Institute, an association of lawyers, judges, and law professors that created the Model Penal Code, a model law on which the criminal laws of nearly half the states are patterned, opposes enactment of mandatory sentencing laws. So does the American Bar Association. Many U.S. federal judges favored repeal of federal laws calling for mandatory sentences in drug cases.

Despite this opposition, it took a U.S. Supreme Court decision rather than an act of Congress to reduce the absolutism of the federal guidelines. In 2005 the Court ruled that the guidelines violated the Sixth Amendment because any fact that increases the penalty for a crime beyond the prescribed statutory maximum must be submitted to a jury and proved beyond a reasonable doubt. The sentencing guidelines violated this principle because judges could increase sentences by applying aggravating factors that the jury never considered. Having made the guidelines advisory, the Court also ruled that the guidelines must still be consulted by judges to help them fashion valid sentences. If a sentence is challenged on appeal, the federal courts must determine if the sentence was reasonable. This decision has set in motion challenges to state sentencing guidelines.

OBJECTIONS TO MANDATORY SENTENCING LAWS

Opponents of mandatory sentencing laws oppose them for a variety of reasons. Many judges and lawyers believe that mandatory sentencing laws are arbitrary and sometimes require judges to impose sentences that are unduly harsh. They think that justice requires that sentences be individualized to fit the circumstances of the offender and of the crime. They also think that sentences should vary depending on considerations such as whether the offender was a ringleader or a follower; whether the offender played a major role or a minor one; whether he or she was motivated by greed or poverty; whether a seller of drugs was an addict raising money to support a drug habit or a professional drug dealer; and whether the quantity involved was large or small. A law requiring that anyone convicted of selling more than a small amount of heroin receive a five-year prison sentence ignores all such distinctions.

Opponents also complain that mandatory sentencing laws adversely affect court operations. Because prosecuting attorneys decide what charges to file in each case, mandatory sentencing laws shift power from the judge to the prosecutor. Most crimes are not covered by mandatory sentencing laws. Typically, for example, trafficking in drugs is subject to mandatory penalties, but possession of drugs is not. Since nearly every drug trafficker also possesses drugs, prosecutors can decide which charge to file; a trafficking charge ties the judge's hands; a possession charge gives the judge discretion.

Another objection is that mandatory penalties remove much of the defendant's incentive to plead guilty and thus increase the frequency of trials and lengthen the time required to resolve cases. In most courts, 85 to 95 percent of convictions result from guilty pleas. Many result from plea bargains, in which the prosecutor agrees either to dismiss some charges or to approve a particular sentence if the defendant pleads guilty. If mandatory penalties remove incentives from plea bargains, then trials, backlogs, and delays increase. Yet another objection is that mandatory sentencing laws sometimes result in deceptive practices on the part of judges. To avoid imposing sentences that they believe are too severe, judges sometimes ignore the mandatory sentence law and impose some other sentence or acquit defendants of crimes that bear mandatory penalties.

In the context of drug laws, the controversy over disparate mandatory minimum sentences for dealers of crack and powder cocaine raged from the late 1980s until 2007. Under a 1986 federal law, one gram of crack is equivalent to 100 grams of powder cocaine. The U.S. Sentencing Guideline Commission

adopted this ratio when it revised its guidelines that year. However, in 1988 Congress amended the law to establish mandatory minimum sentences for cocaine dealing. Thus, selling five grams of crack cocaine is punishable by a mandatory minimum sentence of five years. To receive the same sentence for trafficking in powder cocaine, a defendant would have to sell 500 grams. This resulted in longer prison sentences for small-time crack dealers than for cocaine wholesalers. The federal law and similar state laws have been challenged as violations of equal protection, as African Americans have been charged with more crack cocaine offenses than whites. Similarly, whites have been charged with selling powder cocaine more often than African Americans.

These legal arguments met with little success. By the mid-1990s, the U.S. Sentencing Guideline Commission sought to reduce the disparity in sentencing. Finally, in 2007 the commission modified the guidelines, reducing the sentence range for first-time offenders possessing five grams or more of crack cocaine to 51 to 63 months. The old range was 63 to 78 months. The new range for first-time offenders possessing at least 50 grams is 97 to 121 months in prison, decreasing from 121 to 151 months. A commission analysis estimated that changing the crack guidelines would reduce the size of the federal prison population by 3,800 in fifteen years. The commission also asked Congress to repeal the mandatory prison term for simple possession and increase the amount of crack cocaine required to trigger five-year and ten-year mandatory minimum prison terms. The commission contended this was a way to focus on major drug traffickers.

ARGUMENTS FOR MANDATORY SENTENCING LAWS

Supporters of mandatory sentences are not troubled by the harshness of the laws or the fact that they shift power from the judge to the prosecutor. One of the goals of such laws is to assure that the mandated sentence will be imposed whether the judge agrees with the sentence or not. Supporters are troubled by deceptive efforts of judges (and sometimes of prosecutors) to avoid applying them. They argue that judges are wrong to try to circumvent mandatory sentences, that if legislatures pass laws, judges should enforce them whether or not they agree with them. Finally, supporters say they regret that mandatory sentencing affects guilty pleas, trial rates, and court delays, but they regard those problems as a price worth paying.

Proponents of mandatory sentencing laws make four arguments. First, they argue that the laws allow legislators to assure citizens their concerns are being taken seriously. Second, they assert that harsh mandatory sentencing laws deter offenders from committing crimes. Third, they claim that certain crimes are so serious that people who commit them should be severely punished and that legislators should insist judges impose severe penalties in such cases. Fourth, they contend that mandatory sentencing laws are a device for assuring that offenders who commit the same crime will receive the same penalty.

RESEARCH ON MANDATORY SENTENCING LAWS

Evaluations of mandatory sentencing laws offer greater support to their opponents than to their supporters. Studies on the deterrent effect of mandatory sentencing laws conclude either that passage of such laws has no deterrent effect or that they have a modest deterrent effect that soon disappears. Research on how mandatory sentencing laws affect court operations shows that such laws do shift power from judges to prosecutors, do sometimes result in lower guilty plea rates and higher trial rates, often cause case processing delays, and frequently result in imposition of sentences that the judges and lawyers involved believe are harsher than the defendant deserves. All of these conclusions were reached by the evaluators of the Rockefeller Drug Laws in New York State in the mid-1970s, yet the laws remain on the books despite widespread criticism.

The conclusions of earlier research were confirmed by the most ambitious and sophisticated study of mandatory penalties ever completed: a report on mandatory penalties in the U.S. federal courts by the U.S. Sentencing Commission. That study concluded that people convicted of crimes subject to mandatory penalties were two and one-half times more likely to be convicted after trials (30% of convictions) than are other federal defendants (12.5%). The study found that "mandatory minimums transfer sentencing power from the court to the prosecutor," that "honesty and truth in

sentencing" are compromised by prosecutors' and judges' efforts to work around mandatory sentences, and that "lack of uniform application [of mandatories] creates unwarranted disparity in sentencing."

Thus, on the major empirical issues about which opponents and supporters of mandatory penalties disagree, the great weight of the evidence supports opponents' views. Empirical evidence, however, cannot refute supporters' normative claims that mandatory penalties should be enacted to assure citizens that their concerns about crime are taken seriously or that certain crimes deserve severe punishment and that mandatory sentencing laws should be enacted to increase the likelihood that such punishments will be imposed. Opponents of mandatory penalties do not necessarily disagree that lawmakers should try to respond to citizens' concerns or that some crimes deserve harsh penalties; they do believe that mandatory penalties are an ineffective way to achieve those goals. In addition, the costs of long small-term incarceration continue to take large bites out of state revenues as correctional agencies struggle to house the steady flow of prisoners convicted of drug crimes.

See also **Civil Commitment; Drug Laws, Prosecution of; Legal Regulation of Drugs and Alcohol; Treatment Accountability for Safer Communities (TASC).**

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MARIJUANA (CANNABIS).

Marijuana is the most common name used in the United States for the *Cannabis sativa* plant, which is one variety of the cannabis or hemp plant family. *Cannabis* is the more appropriate scientific term and the more common term used throughout the world to refer to the various psychoactive products derived from the *Cannabis sativa* plant that are used by humans to alter their state of mind. Slang terms for marijuana and other psychoactive products derived from *Cannabis sativa* change over time but some stable and more current terms include: weed, pot, herb, grass, reefer, Mary Jane, dagga, bhang, Aunt Mary, skunk, boom, gangster, kif, ganja, hashish, and hash oil. Cannabis remains in the early twenty-first century the most widely used illicit substance in the United States and in most other developed countries that regulate marijuana. Between the late 1960s and 2008, marijuana use has generated continued controversy regarding its addictive potential, health consequences, potential for medical use, and legal status.

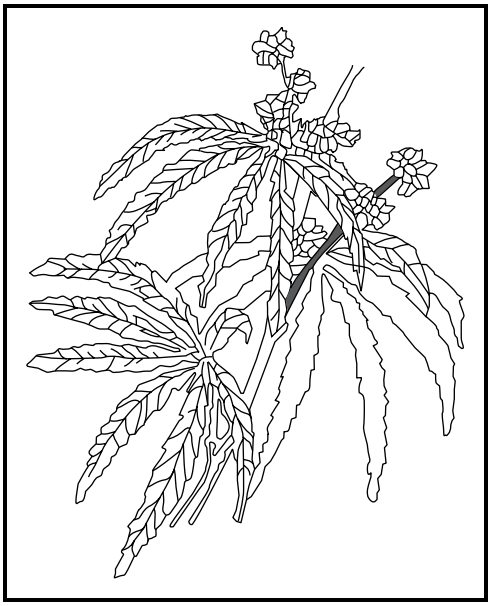

Figure 1. Marijuana. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

THE CANNABIS PLANT

Cannabis sativa grows easily throughout the tropics, subtropics, and temperate regions. It can also grow in colder climates with a shortened growing season. As of 2008 it was grown in most states across the United States. Once established, the plant can reseed and spread. Marijuana comes from the dried flowering tops (buds or heads), leaves, and stems of the harvested plant. The primary mind-altering ingredient in cannabis is delta-9-tetrahydrocannabinol (THC). The THC concentration (strength of the marijuana) partially depends

upon growing conditions and the genetics of the plant. Generally, THC concentration is greatest in the buds, then the leaves, and finally the stems and seeds. Sophisticated growing techniques and breeding of alternative genetic strains have resulted in producing more potent marijuana, with potencies of that confiscated in the first decade of the twenty-first century by legal authorities in the United States and of other samples tested in the Netherlands ranging from approximately 2 percent to more than 20 percent.

Hashish or *hash* is another way that Cannabis sativa is prepared for use. Hash consists of dried cannabis resin and compressed flowers. Its THC concentration is usually 2 to 8 percent, but can get as high as 10 to 15 percent. Extracting THC from hash or marijuana using filtering and purification processes produces hash oil, and its concentration of THC can range from 20 to 60 percent.

USING CANNABIS

The most popular way to use cannabis and hash is by smoking (inhaling) it in pipes or rolling it in cigarette papers (joints, reefers, doobies, spliffs). Water pipes or bongs (a type of pipe) are also used because they cool the smoke and there is not as much marijuana lost through smoke that escapes when a standard pipe is used. Another method for smoking that has become common is rolling cannabis into an emptied cigar casing. This product is usually called a *blunt*, and has become popular because it looks like a legal substance, it can be re-lit easily, and some people report enjoying the effect of the mixture of marijuana and tobacco. Note that the term *spliff* also can be used to refer to a cigarette that is a mixture of marijuana and tobacco. Hash is also typically smoked in some form of a pipe, and hash oil is usually used by adding a few drops to a cigarette or to the mixture in a pipe. Also, the oil can be heated by itself and the vapors inhaled. Marijuana or hash can also be taken orally (eaten), and usually eating has involved cooking or baking it in foods (e.g., brownies). When eaten, the onset of the effects is delayed by about an hour because the drug needs to be absorbed through the stomach, but the effects can last several hours longer.

HISTORY

The use of cannabis as a medicine dates back to the third millennium BCE in China, and to the second and first millennia BCE in India and ancient Assyria. This drug's history offers a collage of medicinal, agricultural, industrial, religious, cultural, and political tales, each of which can be traced back over many centuries. In his 1980 book, *Marihuana: The First Twelve Thousand Years*, Ernest Abel notes:

> Armies and navies have used it to make war, men and women to make love. Hunters and fishermen have snared the most ferocious creatures, from the tiger to the shark, in its herculean weave. Fashion designers have dressed the most elegant women in its supple knit. Hangmen have snapped the necks of thieves and murderers with its fiber. Obstetricians have eased the pain of childbirth with its leaves. Farmers have crushed its seeds and used the oil within to light their lamps. Mourners have thrown its seeds into blazing fires and have had their sorrow transformed into blissful ecstasy by the fumes that filled the air.

In the United States, approximately 30 cannabis preparations, including Chlorodyne, a concoction of morphine and cannabis, were marketed in the 1930s. Superior medications eventually became available, and the drug was removed from the *U.S. Pharmacopoeia and National Formulary* in 1941.

Periodically, commissions of inquiry, for example, the 1925 Panama Canal Zone Committee and the 1944 Mayor's Committee on Marihuana (The LaGuardia Committee), were formed to assess the degree of risk posed to public health by recreational cannabis use. A movement grew to prohibit cannabis possession, and by 1937, when the federal Marijuana Tax Act was passed, all states had banned the drug. The Vietnam antiwar movement saw a substantial increase in the drug's popularity, particularly among young adults in the United States. In reaction to the long prison terms being imposed for possession, the National Commission on Marihuana and Drug Abuse recommended in 1972 that cannabis possession be decriminalized. In that decade a number of states replaced prison terms with either civil penalties or misdemeanor fines. While cannabis remained classified under federal law as having high risk and no accepted medical use, the last decades of the twentieth century saw a number of states enacting laws designed to protect patients from prosecution if a physician recommended use of cannabis. In 1999 the Institute on Medicine released a comprehensive report on the status of marijuana as a recreational drug and its potential for use as a medicine.

CHEMISTRY / PHARMACOLOGY

Cannabis sativa contains over 400 chemical substances. The compounds responsible for most direct effects are called cannabinoids, and over 66 such cannabinoids have been identified. The three most abundant are cannabidiol, tetrahydrocannabinol (THC), and cannabinol. Delta-9-THC is the compound that causes the most notable effects of cannabis. Cannabidiol and cannabinol do not appear to have strong psychoactive properties, but it is thought that they may modify the effects of THC. The proportions of these cannabinoids can vary among strains and can be modified by breeding, resulting in cannabis with different effects and varying potencies.

The effects of THC result from its ability to activate receptors on the surface of specific cells in the brain and body. In the late 1980s it was discovered that humans and animals have an endogenous cannabinoid system, indicating that THC interacts with a naturally occurring system in the body. Two specific types of cannabinoid receptors have been identified (the CB1 and CB2 receptors). CB1 receptors are located primarily on nerve cells in the brain and spinal cord, as well as in some tissues outside the brain. CB2 receptors are located mostly on cells of the immune system and do not appear to be present in the brain. An endogenous cannabinoid, anandamide, has also been identified. The role of the cannabinoid system has only begun to be explored. The effects of cannabinoids known from animal and human experiments include appetite modulation, pain relief, impairment of memory and the control of movements, and reductions in body temperature and in the activity of the gut. Research on cannabinoid pharmacology continues to grow rapidly in the early twenty-first century, and promises to facilitate the understanding of the role of endogenous cannabinoids and the effects of cannabis.

DIRECT EFFECTS AND PSYCHOPHARMACOLOGY

Approximately 30 percent of the THC is delivered into the blood stream when cannabis is smoked. A lower proportion of THC is absorbed after taking cannabis by mouth because THC is metabolized in the liver, but its metabolite is also psychoactive and thus likely prolongs its effects. THC is distributed widely throughout the body via the bloodstream and is stored primarily in fatty tissues. The effects of smoking marijuana are felt within minutes, with maximal effects typically experienced thirty to ninety minutes after smoking. The effects of eating marijuana are usually not felt for about thirty to sixty minutes, and they peak 120 to 240 minutes after ingestion. The direct effects of smoked marijuana may persist for approximately four to six hours; effects following oral consumption may last six to eight hours. The slow release of THC from fatty tissues produces low levels of THC metabolites for many days but no significant effects appear to be caused by such release. Nonetheless, storage and slow release from fatty tissues result in THC being detectable in urine for long periods of time (up to a month) following its ingestion.

When THC enters the brain, it activates the release of dopamine, a neurotransmitter, which is important because dopamine release is associated with the rewarding properties of most drugs and thus may contribute to repeated use and perhaps addiction. Marijuana's actions include a wide range of fairly diverse effects. Indeed, it is difficult to classify marijuana into other common drug categories. In most classification systems, marijuana is either placed in its own category or included with the hallucinogens.

Although wide variation in the effects of marijuana is observed based on an individual's previous experience with the drug, the dose smoked or consumed, and the current smoking environment, the early effects are usually more stimulating in nature: feeling high or a mild euphoria; increased silliness, laughter, and talkativeness; having altered perceptual experiences that include a distorted sense of time and more intense experiences of hearing music, seeing colors, watching movies or television, and eating. Some of the effects might not be pleasant. The most commonly reported unpleasant effects are anxiety, panic reactions, fear of going crazy, and depression. At very high doses, the experience may seem more intense, and one may even feel a sense of depersonalization or experience delusions (beliefs not based in reality) or hallucinations (seeing or hearing things that are not there). These more extreme unpleasant psychological effects are usually felt by infrequent users who are less familiar with the effects of marijuana or by people who have eaten or smoked more marijuana than they are used to. Also, using marijuana with a higher THC concentration or that is laced with other substances can cause such effects. These experiences are typically short-lived and stop when the high obtained from marijuana ends.

Subsequent effects of use are more relaxing, and individuals may become more introspective, with thought or concentration requiring more effort, and memory and psychomotor tasks becoming more difficult. Common physiological effects include increased pulse rate, reddening of the eyes, dry mouth, thirst and hunger, and drowsiness.

With repeated and regular use, tolerance to many of marijuana's effects can develop, which means the user may take more marijuana to achieve an effect or feel less effect when using the same amount of marijuana. Different degrees of tolerance develop for different effects of marijuana. For example, tolerance to the increase in heart rate can develop rapidly. Whether substantial tolerance develops to feeling euphoric is debated.

A withdrawal syndrome can occur in many persons who have been using marijuana heavily for a substantial period of time. The symptoms of this withdrawal syndrome appear somewhat similar to that described with tobacco smokers. The most common symptoms reported are: irritability/anger, restlessness, nervousness, sleep difficulties, vivid dreams, and nausea, craving, and depressed mood. These symptoms typically appear within two to four days after stopping regular use and may last two to three weeks.

EPIDEMIOLOGY

Cannabis remains the most widely used illicit substance in most developed countries that regulate its use, and its rate of use is also increasing in developing countries. In the United States, it is estimated that 98 million people (39 percent) have used the drug; 15 million (6 percent) are currently using it (i.e., at least once in the past month); and 3.1 million are using cannabis daily. Cannabis use is most prevalent among adolescents and young adults aged sixteen to twenty-five. Approximately 34 percent of high school seniors and 28 percent of sophomores have used marijuana at least once, and daily use approximates 6 percent and 4 percent among seniors and sophomores, respectively. Although illegal in the United States, marijuana is readily accessible; approximately 40 percent of eighth graders, 73 percent of tenth graders, and 86 percent of twelfth graders report that they know where to get marijuana.

As with other drugs of abuse, cannabis is used more often by males than females. Cannabis is used across all regions of the United States with minimal variance, although some states have significantly higher rates of use than others. Prevalence of use across major ethnic and racial groups is similar, though there is some indication of slightly higher rates among African Americans, American Indians, and those who claim membership in two or more races.

ADVERSE HEALTH, COGNITIVE, AND BEHAVIORAL CONSEQUENCES

Much remains unknown about cannabis. Moreover, proving that the drug's use causes specific adverse effects, rather than their simply co-occurring with those effects or perhaps being an attempt at self-medication to ameliorate those effects, is an ongoing challenge in cannabis research with humans. Alternative explanations can and should be considered viable until well-controlled research necessitates their being ruled out. This caveat notwithstanding, the findings to date warrant mention of the following potential adverse consequences.

Personal Development. The possibility that cannabis use contributes to disturbances in normal adolescent development is of considerable concern. Frequent cannabis use by adolescents is correlated with such negative psychosocial outcomes as poorer academic performance, truancy, and dropping out of school. Teens who initiate use earlier are at higher risk of developing dependence. There are mixed findings concerning the suggestion that cannabis may interfere with normal adolescent brain development.

Cognitive Function. Although the findings are mixed, some studies indicate that heavy and long-term cannabis use impairs memory and executive functioning, with these consequences persisting after cannabis use has ceased. Moreover, there is evidence that the onset of use before age sixteen or seventeen respectively predicts poorer performance in tasks requiring focused attention and lower verbal IQ in adulthood.

Affective and Psychotic Disorders. Brief psychotic episodes that mimic schizophreniform disorders can occur following cannabis consumption and are generally short-lived. Such episodes are more likely following heavy consumption. In those who are susceptible to schizophrenia, cannabis use increases the

likelihood of an acute episode, an earlier relapse, more frequent hospitalization, and poorer psychosocial functioning. There is also evidence that heavy cannabis use can be a contributing factor in the development of psychotic illness in those without such a predisposition, although conclusions concerning this relationship remain contentious.

There appears to be a small but significant risk of major depression occurring in young adults who are current cannabis users. Early onset and frequent use may increase the risk of both anxiety and depression in young adulthood.

Respiratory System. Heavy cannabis smokers have a greater risk of chronic cough, chronic sputum production, wheezing, and episodes of acute bronchitis than nonsmokers. Additionally, cannabis smokers are at an increased risk of such infectious diseases as pneumonia. Bronchial biopsies give evidence of precancerous pathological changes suggestive of an elevated risk of respiratory tract cancers. One New Zealand population-based case control study in adults fifty-five years of age and younger found that the risk of lung cancer increased 8 percent for each year of cannabis smoking. In contrast, a large case control survey in California found no association between cannabis use and these types of cancer.

Cardiovascular System. For individuals with cardiovascular disease, increased stress on the heart due to the effects of cannabis on the circulatory system may increase the risk of chest pain, heart attack, or stroke.

Driving. Due to cognitive and psychomotor impairments when high, drivers who have consumed cannabis are at a modestly increased risk of accidents.

Fetal Development. Subtle disturbances of brain development may result in cognitive impairment in the offspring of women who use cannabis during pregnancy. The impairment may not appear until preschool or school age.

DEPENDENCE (ADDICTION)

Although the concept of dependence or addiction in relation to cannabis has been questioned by some, diagnostic, epidemiological, laboratory, and clinical studies clearly indicate the existence, importance, and potential for harm of cannabis addiction. As with other substances, including alcohol and tobacco, a subset of individuals who try to continue to use cannabis eventually develops what is labeled as dependence or addiction. It is estimated that 9 percent of those who have used marijuana at least once meet the diagnostic criteria for cannabis dependence, which compares to approximately 15 percent for cocaine, 24 percent for heroin, and 32 percent for tobacco cigarettes. More frequent marijuana use results in greater risk for developing dependence, and in heavier users the proportion meeting dependence criteria may be as high as 50 percent. Between 1992 and 2002, the prevalence of marijuana use disorders among adults increased despite a stabilization of overall rates of marijuana use, and both the rates of use and prevalence of disorders increased among adolescents. It appears that the risk of developing cannabis dependence is elevated (one in six or seven) for users who first use the drug at a young age. Compared with adults, adolescent cannabis users qualify for a diagnosis of dependence with a lower frequency and quantity of cannabis consumption. Cannabis dependence as reported by those seeking treatment because of marijuana-related problems appears highly similar to other substance dependence disorders, although it is usually less severe than most others.

TREATMENT

Treatment admissions in the United States for primary cannabis abuse more than doubled between 1993 and 2003, and similar trends have been observed in such other countries as Australia. There is increased recognition that cannabis is a drug that can lead to addiction and significant negative consequences in a subset of those who use it. This awareness has led to the development of cannabis-specific interventions and treatment materials paralleling those used with other substance use disorders. These advances have increased the acceptability of seeking and providing treatment for cannabis dependence, and consequently the number of individuals seeking help has increased. Types of treatments shown to be effective include: motivational enhancement therapy, cognitive-behavioral treatments, contingency management, and various behavioral family-based treatments (for adolescents). However, as with treatment for other substance use disorders, many individuals do not respond well to these interventions; hence, there is a continued need to develop more effective treatment options.

Optimistic expectations for continued enhancements to treatment approaches appear warranted given that behavioral treatments continue to demonstrate incremental gains in efficacy as innovative interventions are evaluated. Furthermore, rapid advances in understanding the neurobiology of cannabis and the cannabinoid system provide further hope for increasingly effective treatment options (e.g., medications).

MEDICAL USE

Cannabis may have beneficial effects for a number of medical conditions. Oral THC has been approved by the U.S. Food and Drug Administration for use as an appetite- and food-intake stimulant in patients with AIDS wasting syndrome and as an antinausea and antiemetic agent in cancer patients receiving chemotherapy. In 1999 the Institute of Medicine and the National Institutes of Health acknowledged the importance of initiating additional scientific study of the risks and benefits of cannabis use and, in particular, the use of smoked cannabis for specific medical conditions. The interest in the benefits of smoked cannabis in contrast to oral THC arises primarily from differences in the pharmacokinetics of these two routes of administration. Through the oral route, THC absorption is slow and variable; and as a result, clinical effects have a slower onset and longer duration than smoked cannabis. In addition, smoked cannabis delivers both delta-9-THC and other compounds (e.g., delta-8-THC and cannabidiol), which may have direct or interactive effects of therapeutic interest. As of 2008, research comparing the efficacy of oral THC and smoked cannabis for various medical conditions was needed.

By 2008 the medicinal effects of cannabis were being studied regarding a number of other conditions, including as pain relief (analgesia), for the treatment of neuromuscular symptoms (tremors, spasms, or loss of coordination associated with multiple sclerosis or other neurological disorders such as spinal cord injury), and for glaucoma (a disorder of the eye associated with increased intraocular pressure). Case studies and laboratory research suggest that cannabis can positively affect these conditions. Unfortunately, research on these conditions and those for which oral THC has been approved had yet to advance to allow (a) a clear determination of the positive and negative effects of smoked cannabis on each condition; (b) comparisons of oral THC with smoked cannabis; and (c) a comparison of smoked cannabis with other types of medications or medical treatments.

As of 2008, much more data on the effectiveness of smoked cannabis and oral THC for various medical conditions were expected to become available because a number of funding sources had initiated focused efforts to stimulate research in this area. Of additional importance, there was much optimism that additional advancements in research on the newly discovered cannabinoids and the cannabinoid system would result in the development of effective alternative medications that could accentuate the positive effects of cannabis but not produce the other potentially problematic effects of THC and smoke such as sedation, memory problems, intoxication, carcinogens, and respiratory irritation.

LEGAL STATUS

As of 2008, THC was a Schedule I drug (i.e., one that has a high potential for abuse, has no currently accepted medical indication, and for which there is a lack of accepted safety when used under medical supervision). Under the U.S. Controlled Substances Act, a first conviction for cannabis possession can result in a term of imprisonment of not more than one year, a minimum fine of $1,000, or both. A first conviction for trafficking in cannabis (1 to 49 plants) can result in up to five years of imprisonment and a fine of up to $250,000. However, there has been a long history of controversy concerning the drug's legal status. Signatories to the 1961 United Nations Single Convention on Narcotic Drugs agreed to "[a]dopt such measures as may be necessary to prevent the misuse of, and illicit traffic in the leaves of the cannabis plant." Despite the subsequent enactment of prohibition legislation to comply with the Convention, in the latter half of the twentieth century cannabis became the most widely used illicit drug in the Western world.

In the United States in 1972, the National Commission on Marihuana and Drug Abuse recommended that cannabis possession be decriminalized. The Commission members reasoned that overly severe penalties risked undermining the credibility of government in educating the public about potential drug-related harms, and the rationale for decriminalization (i.e., removing criminal penalties for possession while retaining them for selling) was to avoid that consequence while continuing to discourage cannabis use. The Netherlands in 1976,

seeking to distinguish among drugs according to risk level, classified cannabis as a *soft drug*. Possession, cultivation, and sale of small amounts, while remaining illegal, would not be prosecuted. Subsequently, other countries, most notably Canada, Australia, New Zealand, Switzerland, Germany, Spain, Austria, Belgium, Luxembourg, Portugal, Italy, and some U.S. jurisdictions, reduced emphasis on a criminalization approach to cannabis use prevention.

Some people in the United States have argued for full legalization, that is, permitting over-the-counter sale of all drugs. An alternative model that has been suggested is a regulatory system in which cannabis sale is authorized in state-licensed establishments. Proponents of retaining criminal sanctions argue that cannabis use can be harmful and that restrictive laws have effectively kept levels of cannabis use lower than they would be if the drug were to be legalized. Policy reform advocates argue that using criminal penalties to protect users from harming themselves is an unwarranted infringement of individual liberty and that criminalizing cannabis possession has failed to prevent its use.

See also **Adolescents and Drug Use; Cannabis Sativa; Controls: Scheduled Drugs/Drug Schedules, U.S; Driving, Alcohol, and Drugs; Monitoring the Future.**

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MDMA. MDMA (3,4-methylenedioxymethamphetamine) is popularly known as Ecstasy, XTC, and Adam. It is a ring-substituted derivative of the parent compound amphetamine and family member, methamphetamine. The addition of the methylenedioxy ring to the methamphetamine backbone confers its selectivity for binding to serotonin transporters over dopamine transporters. It is also structurally related to the hallucinogen mescaline. Consequently, the pharmacological effects of MDMA are a combination of the effects of the amphetamines and mescaline. These compounds are structurally related to the phenethylamine-type neurotransmitters dopamine, norepinepherine, and epinephrine. Many analogs of these compounds have been synthesized and are sometimes found on the street—the so-called designer drugs.

MDMA was first synthesized in 1912 by Merck; however, the first toxicology studies of the drug were not performed until the 1950s. It was first reported to be psychoactive in humans in 1978. During the 1980s MDMA began to be used in psychotherapy and was reported to increase patients' self-esteem and help facilitate communication with the therapist. Even with these positive effects, in 1985 the U.S. Drug Enforcement Agency classified MDMA as a Schedule I drug due to its high abuse potential, lack of clinical application, and the emerging evidence that it induced serotonergic nerve terminal degeneration in experimental animals. Despite these claims, and since the mid-1980s, MDMA has become a popular club drug, taken at rave parties because of its mild stimulant properties and the sense of euphoria, increased self-esteem, and heightened awareness it induces. Normally taken in tablet form, the average recreational dose of Ecstasy is one to two tablets each containing 60–120 milligrams of MDMA, or a dose of 0.75-4 milligrams/kilograms in a 70-kilogram individual.

Along with the positive subjective effects of MDMA, users have reported adverse physiological effects such as nausea, jaw clenching and teeth grinding, increased muscle tension, blurred vision, and panic attacks. It also causes amphetamine-like stimulation of the autonomic nervous system, producing increases in blood pressure, heart rate, and body temperature. While the drug does not typically result in a hangover, users have reported

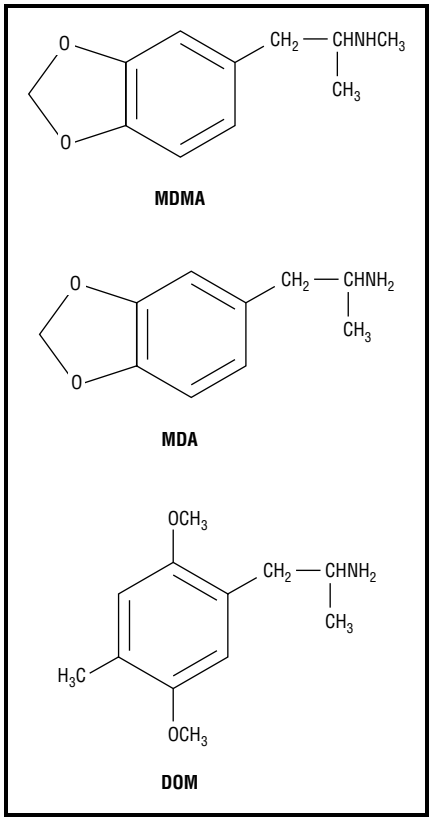

Figure 1. Phenethylamine hallucinogens. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

experiencing midweek blues as well as headaches, insomnia, fatigue, drowsiness, sore jaw muscles, and loss of balance, any of which may last for several days after ingestion. In extreme cases MDMA is lethal due to the pathological consequences of severe hyperthermia (elevated body temperature) as well as liver and cardiovascular toxicity.

Following ingestion, MDMA increases the release of the neurotransmitters serotonin and dopamine by interacting with nerve terminal transporters to cause the outflow of the neurotransmitters and the blockage of their reuptake. These interactions of MDMA with brain serotonergic and dopaminergic systems are likely responsible for its physical, psychological, and behavioral effects.

By the early 1990s increasing evidence indicated that MDMA could damage neurons in the brain. In laboratory animal experiments, MDMA was shown to produce long-lasting reductions in serotonin content in many regions of the brain. More advanced techniques have shown that MDMA causes a destruction of neuronal axon terminals while leaving the cell body intact. Single doses of the drug have been shown to deplete serotonin for several weeks and in some cases serotonin neuron terminals remain decreased for as long as one year after drug administration. In these experiments the extent of serotonin terminal loss appears to depend on the dose and the number of times the drug is administered. The exact mechanisms of MDMA-induced neurotoxicity are unknown at present but studies point to several contributing factors including excessive dopamine and serotonin release, the ability of MDMA to produce hyperthermia, the generation of harmful reactive oxygen species (very small molecules that are highly reactive and thereby damage tissue with which they come in contact), and the formation of neurotoxic breakdown products.

Controversy concerning whether findings from studies in laboratory animals can be applied to human MDMA users have been addressed by several groups. The concept of interspecies scaling suggests that neurotoxic doses of the drug in rodents correspond to recreational doses in humans, if one takes into account the differences in circulation time, organ blood flow and surface area, and liver metabolic enzymes between rodents and humans. Furthermore, increasing evidence suggests that brain function can be altered in humans exposed to the drug. Since the 1990s, considerable research has suggested the presence of cognitive and behavioral deficits associated with long-term MDMA use. Several studies have shown impairments in learning and memory as well as the development of depression and heightened anxiety after heavy MDMA use, all of which appear to correlate with decreases in the number of serotonin transporter sites in the brain as visualized with brain imaging techniques. Based on the implication of serotonergic systems in the control of cognition, sleep, food intake, sexual behavior, anxiety, mood, and the neuroendocrine system, loss of serotonin terminals after MDMA use can have major physical, psychological, and behavioral consequences in humans.

See also **Complications: Mental Disorders; Dopamine; Methamphetamine; Serotonin.**

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MEDIA. Drugs, drug abuse, addiction, and drug traffic have been attractive topics for journalists since about 1900 and nearly as long for screenwriters. As subjects, they incorporate a number of reliable story elements: personal tales of temptation, sin, and redemption (or damnation); the sacrifice of innocents; and lurking (but often unrecognized) dangers. Historically, mainstream media presentations of drug problems (abuse, addiction, and trafficking) have varied along several lines: the drugs in question, the actual incidence of the problems, which demographic groups are using the drugs or seem most at risk; and the overall political climate, which went through several cycles of relative tolerance and intolerance during the twentieth century.

HISTORY OF MEDIA INTERPRETATION AND EMPHASIS

Although media treatments of drug problems have varied over time, they also have been fairly consistent in their use of common themes and language. From the 1920s to the early 2000s, media accounts often described drugs as powerful, seductive, irresistible, and instantly addicting; drug use or abuse was repeatedly termed an *epidemic*, a *scourge*, a *plague*, or a *crisis*. They routinely presented drugs as a direct cause of crime, violence, theft, and other deviant behavior, or as the cause of economic, social, and moral failure. Other common themes included the physical damage caused by drugs, including users' deaths and effects on users' offspring; the association of drugs with various social *outgroups* or minority groups; and drugs as a hidden peril that threatens respectable citizens, professionals, and children.

Prior to 1905, very few articles on drug addiction appeared in the popular press. Americans were much more concerned about alcohol than about other intoxicants between 1820 and 1920. Most of the people writing about drugs such as opium, morphine, and cocaine were physicians and social workers and sometimes missionaries to China. Addict memoirs made occasional appearances as well. These accounts varied in their assessments of the nature and prevalence of addiction.

Popular articles on drug problems increased from 1906 to 1914, and focused on three related drug problems: Opium traffic in China and the Philippines and struggles to establish international controls; domestic efforts to control patent medicines and get dangerous or adulterated products off the market; and increasing cocaine use between about 1907 and 1912. Together, these problems helped justify the passage of the first federal narcotic-control law in 1914. For several years after the passage of the 1914 Harrison Narcotic Act, popular articles were actually quite sympathetic toward the pitiful addicts whose supplies were now curtailed. Some local governments experimented until the early 1920s with heroin maintenance clinics to deal with the problem, and journalists chronicled the efforts of addiction specialists to develop a cure for the victims of addiction. By the mid-1920s, however, antidrug reformers were describing the U.S. *narcotics problem* in apocalyptic terms that later became so familiar. Once regarded as merely unfortunate, drug use was increasingly described as the root of all social evil. By the end of the decade sympathetic accounts of addiction had largely disappeared. The change in rhetoric stemmed partly from genuine increases in addiction and the advent of a new drug (cocaine), but it also had much to do with increasing lower-class recreational drug use and declining middle-class therapeutic use, the success of the alcohol prohibition movement, and the social and cultural effects of the World War I (e.g., xenophobia, fears of Communism, and rejection of traditional culture).

IMPACT OF REFORMERS

The changing media presentations of drug problems after 1920 owe much to the efforts of antidrug activists

such as Richmond P. Hobson (1870–1937). A Spanish-American War hero, former congressman, and well-regarded temperance crusader, Hobson became involved in the campaign against the *dope traffic* in 1920, writing articles and giving talks about the threat of narcotic addiction. He went on to establish several antinarcotic organizations: the International Narcotic Education Association in 1923, the World Conference on Narcotic Education in 1926, and the World Narcotic Defense Organization in 1927. These groups worked hard to raise public awareness, using many of the tactics that had worked so well for the Anti-Saloon League and Woman's Christian Temperance Union against alcohol: enlisting the aid of prominent citizens (e.g., physicians, attorneys, judges, and legislators) and civic organizations, holding national and international conferences, agitating for stricter controls, and sponsoring Narcotic Education Week during the last week in February beginning in 1927. They sent out (by Hobson's account) millions of pamphlets and article reprints, gave interviews, contributed articles to magazines and newspapers, and contacted teachers and school superintendents. Hobson and other reformers such as Sara Graham Mulhall made regular appearances in the *New York Times* and magazines and often gave speeches to women's clubs and other civic groups in New York City. Mulhall published a well-received book (*Opium, the Demon Flower*) in 1926, which was based on her experiences as deputy commissioner of the New York State Narcotic Board. Hobson and his associates were also able to reach a wide audience through the new medium of radio. In all of these forums, the reformers gave wildly exaggerated estimates of the number of drug users, sensational accounts of drug-induced depravity, and gruesome details of the physiological damage drugs caused.

Newspaper Sensationalism and William Randolph Hearst. Hobson and company had an important ally in publisher William Randolph Hearst (1863–1951), and longtime Hearst writer Winifred Black, who wrote under the name Annie Laurie. Black, one of the pioneers of the *sob sister* style of journalism, had been writing exposés for Hearst papers since 1889. It is not clear whether Hearst cared about drug reform before 1920, but he had long used his papers and magazines to promote any cause with a potential for sensation and increased circulation. By 1923, Hearst's media empire was huge, including 22 daily papers (with a total circulation of 3 million), 15 Sunday papers (total circulation of 3.5 million) and 9 magazines (total circulation of 2.7 million). An estimated one of every four American families read a Hearst publication, so any Hearst crusade was guaranteed a large audience. Hearst exerted considerable editorial control over his publications, and, typically, they all ran the same major stories.

Hearst's newspaper crusade against the narcotics threat opened in October 1921, with Annie Laurie's front page *San Francisco Examiner* story, "Drug Evil Invades Cities, Towns, as Ruthless Rings Coolly Recruit Victims." In a month-long series, Laurie detailed the growing menace of efficient, well-organized, cunning drug trafficking rings, whose agents invaded American towns and cities, seducing teenagers and young adults into lives of cocaine and heroin addiction, crime, and squalid degradation. Hearst and his editors wrote frequent editorials (often accompanied by evocative cartoons) likening the *dope problem* to the bubonic plague, urging government to "get after the rats" that spread it. Similar editorials and feature articles continued throughout the decade in Hearst papers (*San Francisco Examiner*, October 21, 1921, p. 24). By 1930, antidrug activists had developed a journalistic template for talking about drug problems that was used with only minor modifications throughout the twentieth and into the twenty-first century.

Federal Bureau of Narcotics and Harry J. Anslinger. Traffic in opiates and cocaine seemed to be coming under control by the late 1920s, and reformers targeted another menacing drug, marijuana, which had escaped regulation under the 1914 Harrison Act and subsequent amendments. In early 1928, the Hearst papers ran a series on the new peril posed by marijuana, which supposedly brought on murderously insane rages in its users. For reformers, and for Harry J. Anslinger (1892–1975), first chief of the Federal Bureau of Narcotics, marijuana was *the* demon drug of the late 1920s and 1930s. Anslinger's position made him the authority of record regarding drugs. He was in great demand for interviews, speeches, and radio addresses on this topic, and co-authored an article titled "Marihuana: Assassin of Youth" for *American Magazine* in July of 1937. His stories of marihuana-induced atrocities and depravity strongly echoed

earlier accounts in Hearst's papers: young men and women with no history of antisocial behavior would, once under the influence of cannabis, ax-murder their families, casually kill strangers and policemen, rob, rape, kidnap, and torture. He also popularized the idea that marijuana use was an inevitable stepping stone to heroin use. The 1936 film *Reefer Madness*, while low-budget and not widely distributed at the time, incorporated many of the themes present in media accounts. Marijuana was outlawed by the 1937 Marijuana Tax Act. Charged with controlling the drug traffic on a very limited budget, Anslinger deftly used the media to present drugs and their users as negatively as possible.

POST-1940S RESURGENCE OF MEDIA ATTENTION

Although stories about drug problems were typically sensational, they were not especially numerous during the 1930s, when Americans were preoccupied with the economic depression and recovery. The topics of drugs and addiction disappeared from the media almost completely during the 1940s; World War II and its aftermath, coupled with federal drug-control efforts disrupted the drug trade for much of that time, and many journalists assumed the drug issue was finished. By late 1950, however, newspapers and magazines were once more running alarming stories about a resurgence of heroin use among teenagers in New York and other major cities, often in conjunction with reports of juvenile delinquency. Initial stories focused on poor minority youths, but journalists soon reported that the problem had left the slums and invaded middle-class schools and neighborhoods. The media accounts were similar in many respects to those in the pre-war years, but several new elements appeared as well. First, there was Anslinger's assertion that Communist China, dumping tons of opium on the world market to raise cash, was behind the phenomenon. Second, many of the articles included statements from addiction researchers at the federal narcotics hospital in Lexington, Kentucky, which introduced the idea that addiction was a chronic relapsing disease suffered by those with an addictive personality. Although the wave of concern over teenaged heroin addicts led to the most stringent narcotics laws yet (the 1951 Boggs Act, which included mandatory minimum sentences for narcotics possession, and the 1956 Narcotics Control Act, which allowed the death penalty for those selling to minors), there was a clear trend toward more sympathetic portrayals of addicts in the media; addict memoirs appeared more frequently, showing users as basically good people who were victimized by their own bad judgment, bad companions, and predatory dealers, and more articles discussed addiction treatment (though facilities were quite scarce at the time).

"Pep Pills" and "Peace Pills": Amphetamine and Meprobamate. The 1950s also brought the first media accounts of several other psychoactive drugs, notably amphetamine and meprobamate. Amphetamine, a stimulant drug developed before World War II, was prescribed as an antidepressant or as a weight-loss aid. Articles about its medical use expressed little concern about abuse or addiction and indeed emphasized its usefulness. Popular literature about non-medical use of the drug was quite different. From the early 1950s, increasing numbers of highway accidents were attributed to truckers' overuse of these *pep pills*, and by 1955 a federal campaign was underway to stop illicit sales to truck drivers. Illicit amphetamines also were featured in articles about thrill-seeking teenagers, who committed various sorts of mayhem while high on *bennies*. In 1957, another media furor resulted from news that recent great athletic feats had been made possible because many of the nation's athletes were "gobbling pep pills (*Time*, June 17, 1957, p. 56)."

Meprobamate (Miltown, Equanil), the first minor tranquilizer, was the subject of hundreds of articles after its introduction in 1954. Many accounts praised its effectiveness, safety, and lack of addictive potential, embracing it as the perfect remedy for keyed-up, tension-ridden, nervous Americans; some even predicted that such drugs might prevent mental illness. The tranquilizers seemed so innocuous during their first decade that some writers dubbed them *peace pills*, *happiness pills*, and *emotional aspirin*. Cartoonists also found tranquilizers to be useful humorous elements, a trend that would continue well into the 1970s. By 1960, when the first benzodiazepine tranquilizer, Librium, appeared, media accounts were more varied. The phenomenal number of prescriptions written (an estimated 8.8 million for Librium alone in 1961, according to the *National Prescription Audit*) prompted worries that tranquilizers were being used as a panacea.

And other writers feared that tranquilizers would completely eliminate "normal healthy anxiety" and divest life of the struggles that properly define humanity (*Reader's Digest*, January, 1957). Pharmaceutical manufacturers, lauded as heroes in the post-penicillin era of drug discovery, were increasingly viewed with suspicion, as profits from tranquilizer sales ballooned.

Concern about psychoactive prescription drugs continued to grow during the 1960s and 1970s, as their use—and, many argued, overuse—expanded. Journalists increasingly blamed the pharmaceutical industry for over-promoting tranquilizers to physicians, and physicians for prescribing the drugs for every complaint. But they primarily blamed middle-class Americans themselves, for expecting to have pills to relieve all of life's ailments and pressing their doctors to furnish them. Media images of other drugs, such as amphetamines and barbiturates (widely prescribed as sleeping aids) became much darker; stories of harrowing side effects (up to and including death) increased, and one widely quoted senator, Thomas Dodd, asserted that the country was in the midst of a "nice-drug epidemic." There was a growing media interest in middle-class addiction, and in the idea of a drug abuse epidemic to which everyone was vulnerable.

Prescription Drugs in the Media. Media coverage of prescription drug problems during the 1970s showed two striking and connected trends: they increasingly focused on women and drugs, and they increasingly portrayed drug users as victims rather than self-indulgent seekers of fast relief. In these accounts, the users were not criminals or thrill seekers, but average Americans, often housewives, being overmedicated by physicians who sought to render them less troublesome and perhaps more conforming to middle-class norms. Many women's magazines ran stories on the dangers of tranquilizer and amphetamine use, focusing on their addictive potential and the large numbers of prescriptions written. At first these emphasized education and better communication between women and their physicians, but by the late 1970s, physicians were under increasing fire for not giving patients enough information, for being dependent on pharmaceutical *detail men* for drug information, and for prescribing instead of listening to their patients. The worst examples of such negligence included the *diet doctors* such as Max Jacobsen (Dr. Feelgood), who had supplied countless politicians and celebrities with the injectable amphetamine they needed to maintain hectic lifestyles, with sometimes tragic results, and the psychiatrist in Barbara Gordon's 1979 memoir, *I'm Dancing as Fast as I Can*, who responded to all of her complaints by prescribing stronger tranquilizers.

Former First Lady Betty Ford provided part of the impetus for this change of focus. In 1978, Mrs. Ford publicly confessed her long-term—and largely invisible—dependence on alcohol, tranquilizers, and other drugs, and encouraged other victims to recognize their addictions and get treatment. A 1975 study conducted by the National Institute of Drug Abuse (NIDA) indicated that women accounted for the majority of *nice drug* prescriptions, lending support to the idea of a hidden drug problem propagated by greedy drug manufacturers and negligent physicians. From this point on, middle-class, non-counterculture addictions were treated sympathetically in popular accounts; for some celebrities, addiction and recovery even became a badge of honor and spawned a new genre of addict memoirs. As their authors did not always limit their substance use to prescribed drugs and alcohol, these memoirs often included tales of various illicit drugs as well.

Late 1960s Counter-Culture "Drug Problems." Mainstream media coverage of counter-culture and recreational drug use during the 1960s and 1970s reflected the varied and often confusing nature of the drug problems that developed during those years. Heroin use increased to worrisome levels during the 1960s, especially among inner-city residents and soldiers returning from Vietnam. Both amphetamines and barbiturates crossed over into illicit markets and, like heroin, were associated with crime and juvenile delinquency. These and relatively unfamiliar drugs such as LSD, peyote, and cocaine also began appearing on college campuses, as did marijuana, embraced as paths to enlightenment or just liberation from societal norms. Especially after the 1967 Summer of Love in San Francisco's Haight Ashbury district, media coverage of drug use increased sharply. Many of these articles emphasized the dangers involved in drug use: the day-to-day degradation of heroin use and addiction; the bad LSD trips that caused users to commit suicide; or the

amphetamine diet pill habit that turned users into emaciated, wild-eyed, violently psychotic *speed freaks*. They also emphasized with alarm the magnitude of the abuse problem, the villainy of drug dealers, and, usually, the extreme addictiveness of the drug, as had journalists in earlier eras.

However, the articles from about 1965 to 1980 were marked by an unusual level of tolerance. Public perceptions of addicts as dangerous deviants had waned by the early 1960s, to be replaced (if briefly) by a more compassionate attitude. In 1962, the Supreme Court ruled that addiction is a disease, not a crime; the following year, a presidential commission recommended that penalties for narcotics offenses be reduced, and funding for addiction treatment increased. This action was in keeping with the overall approach taken toward social problems during the Kennedy and Johnson administrations. So, even as they recounted the horrors of drug addiction to readers, writers also discussed addiction as a disease that could be amenable to treatment. In 1971, President Richard Nixon, declaring that drugs were "public enemy number one," further legitimized this approach by vastly increasing funding for treatment (including methadone maintenance) and education as part of his antidrug initiative (Massing 1998, p. 112). Likewise, popular accounts stressed the importance of education and parent-child communication in combating the various drug epidemics. In the process, they often confused and conflated the various abused drugs and their different pharmacological effects and abuse patterns, probably misinforming as they tried to educate.

Marijuana in the Late 1970s. Marijuana received a lot of coverage during this era, largely because the experiences of millions of young users seemed to disprove all the *Reefer Madness* horror stories of earlier decades. Debates went on for many years, with opponents, often from the drug-control establishment, maintaining that it had dangerous potential for habituation and was a stepping stone to more serious drug use, and proponents arguing that the drug was benign and should be decriminalized. By 1977, President Carter and some of his drug policy advisors had cautiously considered proposals for decriminalization. This period of tolerance was short-lived; by the late 1970s and early 1980s public sentiment was turning against marijuana and drug use in general, led by an influential parent movement. These grassroots antidrug activists soon enlisted policy advisors and First Lady Nancy Reagan in their campaign for a drug-free nation. The ensuing "Just Say No" and *zero-tolerance* approach to drug use would be fed during the next several decades by alarm not over marijuana, but over cocaine.

LATE TWENTIETH CENTURY DRUG CRISES

Media coverage of drug abuse was dominated by cocaine during the 1980s. Expensive and comparatively scarce during the 1970s, cocaine was not considered a high-risk drug even by many treatment experts. Its scarcity and association with wealthy celebrity parties (plus its pleasant stimulant effects, no doubt) glamorized it and increased demand. By the early 1980s supplies had increased, prices had dropped, and *Time* magazine proclaimed that it was the "All-American drug," the first choice of trendy, upwardly mobile middle-class citizens (July 6, 1981). As use increased, however, so did the number of problems.

In late 1985, stories began appearing about a dangerous new drug, a new smokeable form of cocaine called *crack*. Crack use was increasing rapidly in inner cities, contributing to crime and straining treatment facilities. In June 1986, athletes Len Bias and Don Rogers died of cocaine overdoses, and cocaine was immediately transformed from *glitzy party drug* to *killer* in media accounts. For the next decade it seemed that little else mattered; cocaine, crack, and other illicit drugs rapidly went to the top of editorial and political agendas. During the last half of 1986, approximately one thousand stories on crack cocaine appeared in national newspapers and magazines. *Time* and *Newsweek* each devoted five cover stories to the *drug crisis*. In the month of July 1986, major television networks ran 74 evening news pieces on drugs, and in September the CBS news special *48 Hours on Crack Street* earned the highest newsshow Nielsen ratings in five years (Reeves & Campbell, 1994). Newspapers, magazines, and television programs carried a steady stream of horror stories about the burgeoning crack trade in the inner cities, often accompanied by gang-style violence and killing; about the addicts' rapid descent into a hellish world of crime, prostitution, and crack houses; about the destruction of families and entire neighborhoods by the crack trade; about the

violent behavior caused by the drugs; about the sinister South American drug cartels that kept the traffic going.

Politicians quickly joined the hue and cry and initiated new legislation to "get tough on drugs" (*Newsweek*, August 18, 1986, p. 16). The drug-war budget was greatly increased, and various crime bills and drug control measures imposed mandatory minimum sentences and longer jail terms overall for drug-related offenses. Treatment experts declared that crack was instantaneously addicting, and the confessions of addicts seemed to support this view. The crack problem was widely touted as the most horrible threat the nation had ever faced. More dramatic writers compared U.S. drug use to the bubonic plague of medieval times. *Newsweek*, for example, noted that an entire generation of American youth was "increasingly at risk to the nightmare of addiction," because a "flood tide of cocaine," ("the most glamorous, seductive, destructive, dangerous drug on the supersaturated national black market,") was reaching consumers of all ages in this country (March 11, 1986, p. 58). Within a few years, *crack babies* born to addicted mothers joined the list of victims in media accounts.

Other drugs, such as MDMA (Ecstasy), also captured a fair amount of media attention during the 1990s, but they never eclipsed cocaine as top stories. For a few years after the terrorist attacks of September 11, 2001, not surprisingly, drug abuse and the war on drugs, like many other topics, were largely sidelined except as they related to the war on terror. Subsequently, cocaine and crack lost their media ranking as "America's Most Dangerous Drugs" to methamphetamine, a substance similar in its effects and its abuse patterns. Likewise, media stories about *meth* were similar to earlier accounts of crack cocaine in their tone and emphasis. Addiction science made great progress in the 1970s, exploring the brain chemistry and genetic components of addiction and holding out the hope of better treatment if not cures. Such advances were enthusiastically reported in the media, though they were sometimes used only to buttress the more traditional horror stories. As public enthusiasm for wars on drugs waned, media accounts and policy discussions seemed to enter another cycle of relative tolerance or at least of greater openness to fresh approaches to a perennial problem.

DRUGS IN FILM AND TELEVISION

Like newspaper and magazine accounts, film and television renderings of drug use, addicts, and antidrug enforcers have often reflected cultural climates of tolerance or intolerance. Between 1934 and about 1965, a period of relative intolerance, Hollywood producers and screenwriters were constrained by the Hays Code. Also known as the Production Code, it prohibited the depiction of illegal drug use, along with many other elements that might lower the moral standards of movie audiences. Earlier films did sometimes incorporate drugs as tragic or comic devices, and various non-Hollywood tabloid-type films after the mid-30s dramatized the horrors of addiction, often for educational purposes. Produced before the Hays Code was widely enforced, Charlie Chaplin's 1936 *Modern Times*, in which the hero accidentally pours cocaine on his food with hilarious results, was probably the last film to feature any sort of drug humor until the 1970s. Otto Preminger's *The Man with the Golden Arm* (1955) was released without the Motion Picture Association's approval. The film's depiction of a reformed heroin addict struggling to stay clean was controversial but garnered several Academy Award nominations. Hays Code restrictions were gradually eased during the next decade, allowing drugs, sex, crime, and other risky topics to be featured in movies.

Films during the 1960s and 1970s depicted drug use much more frequently, though addiction *per se* was rarely the main focus (1971's *The Panic in Needle Park* is one exception). More often, the seedy underworld of drug trafficking provided primary or secondary story lines (e.g., 1971's *The French Connection*). In many films, as in newspapers and magazines of these decades, drug use—especially heroin or amphetamine—ended in tragedy. Marijuana use, in keeping with the times, was depicted as part of the youth-culture backdrop, as was cocaine. Though depictions of heroin use might be grim, marijuana and cocaine intoxication furnished comic elements in many films. When the cocaine and crack crisis developed during the 1980s, films mirrored the grim new reality in stories such as *Scarface* (1983) and *Clean and Sober* (1988). Later films featured more graphic descriptions of drug use and addict life (e.g., *Trainspotting* and *Pulp Fiction*.) As in the print media, there was also a trend away from moralizing about drugs,

instead looking with a critical eye at the world created by current policies (e.g., 2000's *Traffic* and television dramas such as *The Wire*).

See also **Epidemics of Drug Abuse in the United States; Internet: Impact on Drug and Alcohol Use; Movies; Music; Parent Movement, The; Zero Tolerance.**

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SUSAN L. SPEAKER

MEMORY, EFFECTS OF DRUGS ON.

Research investigating the effects on memory of alcohol (ethanol) and drugs of abuse is disproportionately small in relation to the widespread use of these substances worldwide. The available evidence clearly indicates that ethanol and abused drugs significantly affect memory processes. Much of the knowledge of the effects of such commonly used substances on memory is based on experiments using laboratory animals. In typical experiments, the animals are trained in a learning task and given a memory retention test after a delay of one day or longer. In experiments on commonly used learning tasks, the animals are trained to acquire responses that provide escape from, or avoidance of, aversive (unpleasant) stimulation. Appetitive motivation (food or water reward) is used to train animals in mazes and other types of spatial learning.

When investigating acute (single treatment) influences on learning and memory, drugs can be administered before the training, shortly after the training, or before the memory test. When drugs are administered before training, it is difficult to differentiate effects on memory from influences on sensory, motivational, and motor processes. When administered within a few minutes after training, but not after a delay of several hours, drugs of many classes can enhance or impair memory. Such findings are interpreted as indicating that the drugs can modulate memory-consolidation processes after a training session. The drug effects are typically dose-dependent. For example, drugs that enhance memory when administered in low doses may impair memory when administered in higher doses. Experiments examining the effects of a drug administered prior to memory testing are difficult to interpret, as drugs can alter many processes affecting behavior other than memory. For the same reasons, the alterations in memory performance that are produced by the chronic (long-term) administration of drugs are also difficult to interpret.

ALCOHOL (ETHANOL)

In rats and mice, an acute one-time dose of alcohol prior to learning usually impairs memory of the training. The effect is heightened by the drug clonazepam, a benzodiazepine receptor agonist; it is lessened by bicuculline and picrotoxin, drugs that block receptors for the inhibitory neurotransmitter GABA (GABA-A receptors). Such findings suggest that ethanol-induced amnesia is mediated by the benzodiazepine/GABA-A receptor complex. These findings are consistent with extensive evidence that benzodiazepines (see section below) induce amnesia in humans as well as in laboratory animals. Memory impairment induced by a large dose of alcohol is also lessened by physostigmine, the acetylcholinesterase inhibitor, suggesting that ethanol influences on memory involve cholinergic mechanisms (i.e., those involving the neurotransmitter acetylcholine).

Chronic administration of a high dose of ethanol to rats or mice over time induces memory impairment, accompanied by a decreased function of specific brain regions, including the hippocampus and neocortex. The syndrome can be reversed by an implant, into either brain structure, of fetal brain tissue that has high numbers of cholinergic cells or by giving oxotremorine, the cholinergic muscarinic

agonist (i.e., an agent that simulates the actions of acetylcholine), prior to memory testing. Such findings suggest that the memory impairment resulting from chronic ethanol ingestion is associated with a deficit of brain cholinergic function.

Acute or chronic ethanol ingestion in humans also produces memory problems. Large amounts of ethanol taken over a short period (hours or days) may cause a severe amnesia—a *blackout* for events occurring during and/or shortly before the period of intoxication. Some alcoholic blackouts may be partially state dependent—that is, during a later intoxication, individuals may sometimes remember experiences that occurred during a previous blackout. This phenomenon was illustrated in Charles Chaplin's 1931 film *City Lights*, in which the hard-drinking millionaire remembered Charlie only when under the influence of alcohol. Some drinking patterns may have a more harmful effect on brain function than others. Research has shown that college students who binge drink (i.e., episodically drink heavily) perform more poorly on cognitive tests, most notably measures of working memory, than non-binge drinkers who consume the same amount of alcohol, but do so more moderately but more frequently. Working memory refers to the process of storing and manipulating information and involves frontal lobe brain systems. The mechanism for this is not known, but binge drinking may have effects similar to those of repeated episodes of alcohol withdrawal, which is associated with cognitive impairment in alcoholics undergoing recovery. Moreover, the effects of binge drinking on brain function seem to be greater among women.

Studies of alcohol-related brain dysfunction have quantified what has been known for hundreds of years, namely that chronic alcohol use can have a harmful effect on human memory. The most severe forms of alcohol-related memory loss are Korsakoff's syndrome and alcohol dementia. Korsakoff's syndrome is due to Vitamin B_1 (thiamine) deficiency, resulting from poor food intake during sustained periods of alcohol consumption and reduced absorption of the vitamin due to the adverse gastrointestinal effects of heavy drinking. Korsakoff's syndrome is characterized by profound memory loss and impaired executive functioning, but relatively normal IQ scores. Alcoholics who meet the usual *DSM-IV* criteria for dementia, including profound amnesia without preserved intelligence, are often given the diagnosis of alcohol dementia, although some consider alcohol dementia to be the result of multiple causes. Improvements in such patients are seen if they abstain from alcohol. However, most memory deficits are permanent.

It is not known whether the deficits seen in early alcohol dementia and in Korsakoff's syndrome are accompanied by alterations in GABAergic or cholinergic functioning. The changes seen in late alcoholic dementia, like those of Alzheimer's disease, involve multiple focal (in particular regions) brain lesions, primarily in the temporal lobe but also in other brain regions, and involve deficits in glutaminergic, GABAergic, and cholinergic systems.

Large-scale studies of non-demented alcoholics in treatment have shown that, during the intermediate abstinence period, which begins after detoxification and extends through the first two months of abstinence, as many as half of recovering alcoholics have measurable brain abnormalities and cognitive deficits, including memory loss. Significant recovery with continued abstinence is typical. However, there is considerable variability among patient populations depending on the age, health, and presence of comorbid psychopathology.

BENZODIAZEPINES

Benzodiazepines are used clinically in the treatment of anxiety and the induction of sleep. These drugs have also been widely abused. It has been known for several decades that benzodiazepines, including diazepam (Valium), triazolam (Halcion), and chlordiazepoxide (Librium) impair the creation of new memories in humans. Studies using laboratory animals indicate that benzodiazepines impair memory when administered before training, but they generally do not impair memory when administered after training. The lack of post-training effects may be due, at least in part, to the fact that benzodiazepines are absorbed slowly and are slow to reach peak concentrations in the brain following peripheral injections.

Benzodiazepines act by modulating GABA-A neurotransmitter receptors on the benzodiazepine/GABA receptor complex. Their effects on memory appear to be mediated primarily by the brain structures designated as the amygdaloid

complex and hippocampus. When administered acutely (one-time dose), either into the system or directly into specific brain regions, including the amygdaloid complex and the hippocampus, immediately following training, retention is enhanced by flumazenil, the benzodiazepine-receptor antagonist, and by the GABA-A-receptor antagonists (blockers) bicuculline and picrotoxin. Findings indicating that the amnesia induced by peripherally administered benzodiazepines is blocked by GABAergic antagonists administered directly into the amygdaloid complex, as well as by lesions of the amygdaloid complex, provide additional evidence that this brain region is involved in benzodiazepine effects on memory. Although benzodiazepine-like substances are found in the brain, it is not yet known whether they are synthesized in brain cells or derived from food. Evidence that training releases these naturally occurring substances in the brain suggests that they may play a role in modulating memory-storage processes.

MARIJUANA

In laboratory animals, both acute and chronic administration of marijuana extracts or of their active agents, the tetrahydrocannabinols (THC), have been reported to impair the acquisition and retention of a wide variety of tasks. It is not known whether these effects are due to influences on memory or simply to the sedative effects of the drug. There is also evidence that chronic exposure to the chemicals found in marijuana produces permanent working memory impairment in adolescent but not adult rats, suggesting an interaction with brain development.

Evidence suggests that acute and chronic use of marijuana affects human memory beyond the period of intoxication. Memory deficits have been detected for up to seven days after heavy marijuana use but were reversed with sustained abstinence. Years of long-term marijuana abuse appear to produce memory loss during abstinent periods. Although the mechanism is not well understood, some evidence shows that THC affects neuronal functioning in the prefrontal cortex and hippocampus, two regions critical for normal memory.

OPIATES AND OPIOID PEPTIDES

The opiate drugs morphine and heroin, administered after training, impair retention in laboratory animals. Opiate-receptor antagonists, including naloxone and naltrexone, enhance memory and block the memory impairment produced by opiates. Endogenous opioid peptides (brain peptides that mimic the effects of morphine, heroin, and other opiates) also affect memory. The opioid beta-endorphin is released in the brain when animals are exposed to novel training situations. Post-training injections of beta-endorphin cause memory impairment as do injections into several brain regions, including the amygdaloid complex and medial septum. Opiate antagonists administered into these brain regions enhance memory. Under some conditions, beta-endorphin administered (or released by the individual) prior to memory testing may lessen the memory impairment induced by a post-training injection of the peptide.

Despite the widespread and long-standing use of opiate drugs by humans, there have been no systematic studies on the effect of morphine, heroin, or other opiates on human memory. Chronic opiate users do show memory deficits, but these may result from general deterioration rather than from any specific effect of the opiates. Acute administration of opiates (as in pre-anesthetic medication, for example) may induce a temporary amnesia. The failure of patients to remember experiences immediately prior to surgery may be due, at least in part, to an effect on memory of the opiates used for pain suppression. The effect of opiate antagonists for the treatment of dementias has been studied, but with limited success.

AMPHETAMINE

In laboratory animals, chronic administration of amphetamine prior to training impairs performance in many types of learning tasks. Such effects are typically obtained in experiments using high doses of amphetamine and complex learning tasks. In contrast, extensive evidence from studies using a variety of training tasks indicates that acute post-training injections of amphetamine produce enhancement of memory depending on the size of the dose. Retention is also enhanced by direct administration of amphetamine into several brain regions. Amphetamine acts by releasing and blocking the reuptake of the catecholamines epinephrine, norepinephrine, and dopamine from cells. Amphetamine effects on memory appear to result primarily from influences

on brain dopaminergic systems as well as through the release of peripheral catecholamines.

Amphetamine users often report that their "learning capacity" is enhanced by single doses of the substance. Because there are few systematic and well-controlled studies of the effects of amphetamine on memory in humans, however, it is not known whether such reports reflect subjective changes in perception and mood or actual effects on memory. Chronic amphetamine use is usually accompanied by a deterioration of memory function, an effect that subsides with cessation of use.

COCAINE

Despite the extensive use and abuse of cocaine, little is known about cocaine effects on memory. Results of studies using rats and mice indicate that acute post-training administration induces dose-dependent effects comparable to those of amphetamine: Memory is enhanced by low doses and impaired by higher doses. The brain processes affecting cocaine influences on memory have not been extensively investigated. The effects appear to be mediated by influences on noradrenergic and dopaminergic systems. Also, as with amphetamine, cocaine users report that memory is enhanced by one-time doses, but impaired by chronic use. Systematic, well-controlled studies of the effects of cocaine on human memory are lacking.

The effects on memory and intellectual functioning of other drugs—such as phencyclidine (PCP), barbiturates, nicotine, and inhalants—are considered in connection with these agents and in separate articles.

See also **Abuse Liability of Drugs: Testing in Humans; Agonist; Alcohol: Chemistry and Pharmacology; Amphetamine; Analgesic; Antagonist; Anxiety; Barbiturates; Benzodiazepines; Brain Structures and Drugs; Cannabinoids; Catecholamines; Chlordiazepoxide; Cocaine; Complications: Cognition; Coping and Drug Use; Drug Interaction and the Brain; Endorphins; Gamma-Aminobutyric Acid (GABA); Heroin; Inhalants; Morphine; Naloxone; Naltrexone; Neurotransmitters; Nicotine; Opiates/Opioids; Phencyclidine (PCP); Productivity: Effects of Alcohol on; Research, Animal Model: An Overview; Research: Measuring Effects of Drugs on Behavior; Risk Factors for Substance Use, Abuse, and Dependence: Learning; Synapse, Brain; Wikler's Conditioning Theory of Drug Addiction.**

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MEPERIDINE. Meperidine is a totally synthetic opioid analgesic (painkiller) with a structure quite distinct from that of morphine, a natural opiate. Unlike morphine's rigid fused ring structures, the structure of meperidine is flexible; it is a

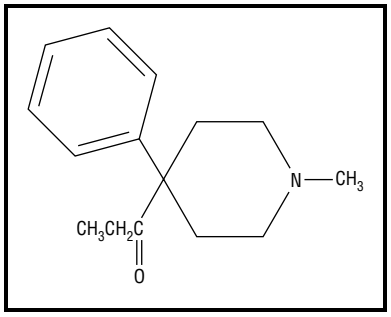

Figure 1. Chemical structure of meperidine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

phenylpiperidine and bends so that the key portions of the molecule can assume positions similar to those of morphine. A number of other compounds with similar structures are widely used in medicine, including loperamide (used primarily for treating diarrhea) and the extraordinarily potent analgesic agents fentanyl, sufentanil, lofentanil, and alfentanil (for treating pain).

Meperidine is a compound with strong analgesic effects similar to morphine's, although greater amounts are needed to produce the same level of analgesia. It is one of the more commonly prescribed opioid analgesics and is better known under one of its brand names, Demerol. Given by injection, 100 milligrams of meperidine equals 10 milligrams of morphine. Meperidine can be administered orally as well as by injection; but its potency it not as great following oral administration, so the dose must be increased proportionally. Like morphine, continued use of meperidine is associated with decreased analgesia—tolerance—as well as physical dependence. As with the other opioids, addiction (defined as a drug-seeking behavior) is not commonly observed with this drug when used for medicinal purposes, but meperidine is highly valued on the street and is widely abused, particularly in its injectable forms.

Medically, meperidine is a significant problem in patients with kidney conditions, in which drug-removal from the body is impaired. Metabolized to normeperidine, a closely related compound, it is eliminated by the kidneys. In patients with kidney problems, this metabolite can accumulate to high levels that can cloud mental processes and even produce convulsions. Since elderly patients often have impaired kidney function, special care must be taken when using meperidine with them.

See also **Addiction: Concepts and Definitions; Opioid Complications and Withdrawal.**

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GAVRIL W. PASTERNAK

MEPROBAMATE. Meprobamate is a sedative-hypnotic drug that is now typically used to treat muscle spasms. Meprobamate is prescribed and sold as Deprol, Equagesic, Equanil, Meprospan, and Miltown. Because of its abuse potential, it is included in Schedule IV of the Controlled Substances Act. It was first introduced into clinical medicine in 1955 for the treatment of anxiety. At the time it was thought to have specific antianxiety effects and to be quite different from other sedative-hypnotics. Also introduced at about the same time were chlorpromazine (Thorazine), which had remarkable antipsychotic effects, and reserpine, which had tranquilizing as well as blood pressure-lowering effects. These three agents were considered the harbingers of the new era of psychopharmacology and helped popularize the new term *tranquilizer*.

Within a year or two after its introduction, meprobamate had become one of the most widely prescribed drugs in the United States. It was not long, however, before its distinction from other sedative-hypnotic agents was reassessed; and within a decade it was recognized that meprobamate shared many of the properties of such other central nervous system depressants, as the barbiturates. By the early 1960s, its use for the treatment of anxiety was eclipsed by the benzodiazepines. Although it is prescribed as a muscle relaxant, the only use currently

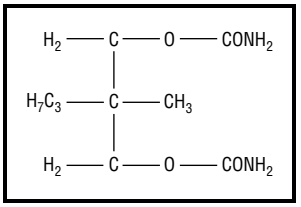

Figure 1. Chemical structure of meprobamate. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

approved in the United States by the Food and Drug Administration is as a sedative-hypnotic.

Meprobamate has a number of side effects, including tremor, nausea, depression, and various allergic reactions. Continued use of high doses can result in tolerance and physical dependence. Convulsions and other signs of withdrawal are reported upon termination of high-dose treatment or inappropriate use.

See also **Anxiety; Barbiturates; Sedative-Hypnotic.**

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MESCALINE. Mescaline is a naturally occurring hallucinogen, one of the oldest psychedelic substances known. It was first obtained from the peyote cactus (*Lophophra williamsii* or *Anhalonium lewinii*), which grows in the southwestern United States and northern Mexico. Peyote buttons, the dried tops of the peyote cactus, were originally used by pre-Columbian Native Americans in those regions as an antispasmodic as well as for highly structured religious rituals; the button was eaten or was steeped to make a drink. It continues to be used in ritual by the Native American Church.

Mescaline is a member of the phenethylamine-type family of hallucinogens, which includes DOM, MDA, and MDMA. The overall behavioral effects

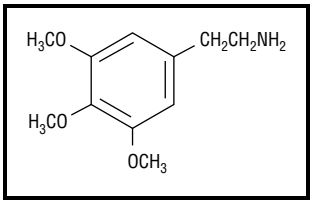

Figure 1. Chemical structure of mescaline. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

of mescaline are very similar to those produced by lysergic acid diethylamide (LSD); however, it is approximately 100 to 1,000 times less potent than LSD, although the effects of mescaline last from 10 to 12 hours.

See also **Psilocybin; Religion and Drug Use.**

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METHADONE MAINTENANCE PROGRAMS. The history of methadone treatment offers a striking example of the benefits and limits of research findings on public attitudes and policies regarding methadone maintenance treatment. To understand methadone maintenance treatment, it is necessary to appreciate the profound stigma attached to both patients and treatment providers. This establishes the context for understanding how a modality with the most extensive research base in the addiction treatment field can still engender passionate dispute.

Methadone maintenance was developed as a treatment modality in the mid-1960s by Vincent Dole and Marie Nyswander in response to prevailing concerns about epidemic levels of heroin

addiction and related health problems, mortality (especially among young people 15 to 35 years old), and high relapse rates. Methadone was synthesized in Germany during World War II as a synthetic analgesic, and after the war it was studied at the U.S. Public Health Service Hospital in Lexington, Kentucky. The drug was approved by the U.S. Food & Drug Administration in August 1947 for use in the treatment of pain. Its initial use in the treatment of addiction was to ease withdrawal in individuals being treated for heroin addiction; it was subsequently determined to be well suited to long-term maintenance treatment.

As a treatment tool, methadone provides a safe and effective way to eliminate drug craving, withdrawal, and drug-seeking behavior, thus freeing patients to lead productive lives. In conjunction with educational, medical, and counseling services, it has been thoroughly documented as enabling patients to discontinue or reduce illicit drug use and associated criminal activity, improve physical and mental well-being, become responsible family members, further their education, obtain and maintain stable employment, and resume or establish a productive lifestyle. Yet despite over four decades of research confirming its value, methadone maintenance treatment remains a source of contention among treatment providers, the public, and particularly among officials and policymakers. As an example of this modality's value, a 2002 Cochrane Review concluded that this form of treatment is superior in terms of patient retention and reduction of heroin use to nonpharmacological therapies for opioid dependence (Mattick et al., 2002). Unlike controversies based on a difference of opinion between informed parties, debate about methadone usually involves several common misunderstandings about the drug and its uses.

COMMON MISUNDERSTANDINGS

Much of the uneasiness about methadone stems from the idea that it is "just substituting one addictive drug for another." Indeed, this is technically correct—methadone treatment is drug-replacement therapy in which a long-acting, orally administered preparation is substituted for a short-acting opioid that is used intravenously. The long-acting (24 to 36 hours) effect of preventing withdrawal allows most patients to receive a dose and function in a stable manner, without the four-hour cycles of euphoria and withdrawal that characterize heroin use. The objection that methadone is "addictive" reflects the recognition that the medication produces dependence.

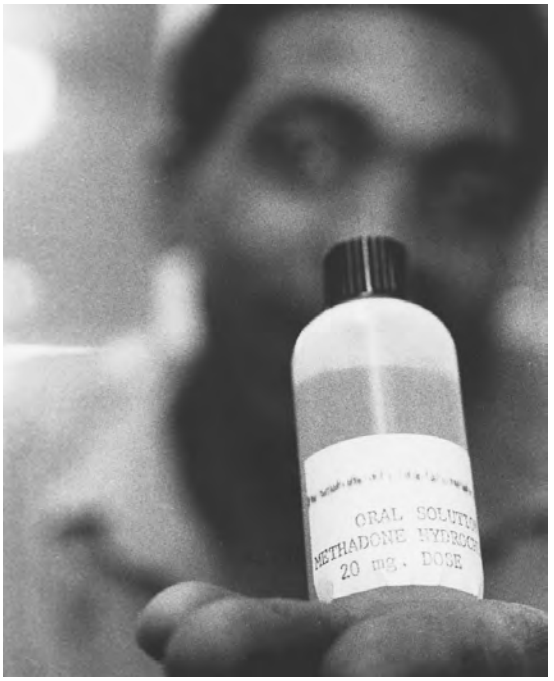
However, addiction treatment professionals increasingly distinguish between physical dependence and addiction, the latter being characterized by behavior that is compulsive and out of control, that persists despite adverse consequences, and where the relationship with the substance is more salient to the addict than anything else. On the other hand patients with chronic pain will develop physical dependence on a drug, though their overall functioning is improved. Appropriate prescribing of benzodiazepines for patients with anxiety disorders is another example of a dependence-producing drug used beneficially for thousands of patients. Although physical dependence is a factor to be considered, the use of methadone provides a neurochemical platform of stability, allowing the patients to reorient their lives so that their relationship with opioids is no longer the central organizing factor of their lives.

Another point of discord is the belief that "methadone keeps you high," a notion that reflects a misunderstanding of the effects of a properly adjusted dose. Once stabilized, most patients experience little or no subjective effects. Indeed, heroin addicts will readily state that they seek methadone to avoid becoming sick (prevent withdrawal effects), not to get high. When the patient's dose is being stabilized, he or she may experience some subjective effects, but the wide therapeutic window allows for the dose to be adjusted to avoid craving (due to an inadequate dose) and somnolence (due to an excessive dose). Dose adjustment may take some weeks and may be disrupted by a variety of medical and lifestyle factors, but once it is achieved the patient should function normally.

There is also ample scientific evidence that the long-term administration of methadone results in no physical or psychological impairment of any kind that can be perceived by the patient, observed by a physician, or detected by a scientist. More specifically, there is no impairment of balance,

coordination, mental abilities, eye-hand coordination, depth perception, or psychomotor functioning, unless the patient is using other impairing drugs or medications (Lenné et al., 2003).

A third point of resistance—the objection to long-term, or even life-long, maintenance—is better addressed following the presentation of some basic information about opioid addiction and the nature of treatment.



Methadone. IAN MILES–FLASHPOINT PICTURES/ALAMY.

HOW DOES METHADONE TREATMENT WORK?

Most addiction specialists agree that addictive disorders are complex phenomena involving the interaction of biologic, psychosocial, and environmental variables, all of which need to be considered to make treatment effective. Dole and Nyswander, who pioneered the use of methadone, held the view that there was something unique about opioid addiction that made it difficult for patients to remain drug-free. Although originally intended as a long-term treatment for a metabolic defect, many initially hoped that methadone could be used to transition heroin addicts to a drug-free lifestyle and then be discontinued. Research in the subsequent decades indicates that less than 20 percent of patients will be able to discontinue methadone and remain drug-free. As his thinking evolved, Dole postulated in 1988 that a receptor system dysfunction resulting from chronic use leads to permanent alterations that medical science does not currently know how to reverse. New brain imaging technology holds the promise of better understanding and, eventually, improved intervention, but in the interim it appears that methadone is corrective but not curative for the severely addicted person. Two important questions for future research are whether a preexisting condition enhances the vulnerability of some patients to addiction, and what the differences are among opioid addicts who respond to short- or intermediate-term treatment versus those who need indefinite maintenance therapy due to permanent brain dysregulation.

Studies indicate that methadone is a benign drug that exhibits stability of receptor occupation and thus permits interacting systems to function normally. One example of this is the normalization of hormone cycles and the return of regular menstrual cycles in women. This distinguishes it from heroin, a short-acting narcotic that produces rapid changes and makes a stable state of adaptation impossible. Although tolerance develops to most effects of methadone, it is fortunate that even long-term use (30 years or more) does not produce tolerance to the reduced craving effect or to the narcotic withdrawal prevention effect.

The desired response to methadone depends on the maintenance of a stable blood level at all times. Appropriate doses usually keep the patient in the therapeutic range of 150 to 600 nanograms per milliliter (ng/mL) in the blood, which produces the stable state so important for rehabilitation. What is referred to as a "rush" or "high" is the result of rapidly changing blood (and brain) levels. Thus, once therapeutic levels are achieved and maintained, the patient experiences little subjective effect.

Unfortunately, negative attitudes toward methadone have historically played a significant role in dosing practices. In particular dose ceilings were imposed by state or local regulations without regard to medical criteria. Such policies placed a value on giving as little of the drug as possible (versus the therapeutic level needed to accomplish the goal), influenced in part by the unsubstantiated belief that lower doses would make it easier to discontinue methadone. It was common to have dose ceilings

of 40 milligrams per day. It is now well established that this is inadequate to maintain the necessary plasma concentrations to be effective—the effective range is between 60 and 120 milligrams per day for most patients, with some needing less than 60 milligrams and others considerably more than 120 milligrams. Higher doses are strikingly well correlated with reductions in illicit drug use and improved retention in treatment (Ward et al., 1998). Subsequent to studies that documented the prevalence of insufficient dose levels in methadone programs in the United States (D'Aunno and Vaughan, 1992), there has been a vigorous effort to educate treatment staff, including program physicians, about proper methadone dosing through publications from the American Society for Addiction Medicine and accreditation guidelines promulgated by the Center for Substance Abuse Treatment in 1999 (and revised in 2007).

Initial hopes that methadone could be used to transition patients to a medication-free lifestyle have proven unrealistic. Studies indicate that although short-term abstinence is common, there are high rates of relapse to opioid use after methadone treatment is discontinued (Magura and Rosenblum, 2001). Moreover, research indicates that indefinite methadone treatment is more cost-effective than a 180-day detoxification protocol (Masson et al., 2004). Clinicians who have worked with this population over the long term believe that although lifestyle changes are essential to successfully discontinuing methadone, such changes in conjunction with high motivation will still be insufficient for most patients, and that neurobiological factors remain a deciding factor. Increasingly, opioid addiction, as with other forms of addiction, are being viewed as chronic medical diseases for which medication-assisted treatment is not curative but rather provides the patients with tools they can use for a healthier life (McLellan et al., 2000). It is to be hoped that this changing conceptualization of addiction will lead patients on methadone to feel less pressure—from family, employers, health and social service providers, fellowship support group members, and themselves—to discontinue methadone treatment prematurely.

METHADONE AND OTHER DRUGS

Methadone patients may engage in alcohol, cocaine, and other drug use prevalent in their communities, even to the level of addiction. It is important to remember that methadone is opioid-specific and does not in itself increase or prevent other kinds of drug use. It does, however, offer the enormous advantage of making the patient accessible to other kinds of intervention. Rules governing take-home medication are intended to reduce the diversion of methadone onto the illicit market. At a minimum, they mandate that the patient initially come to the clinic six days per week, with decreasing clinic visits for dosing achieved over time. Thus, the patient can be exposed to educational presentations and materials, and to counseling interventions as indicated by an individualized treatment plan, which is required as part of the treatment effort.

Cocaine, methamphetamine, and benzodiazepine abuse have received particular attention, because continuing abuse of or addiction to these drugs predict poorer retention in (and response to) methadone treatment. Research and training efforts have been brought to bear on this problem, but the lack of effective addiction medications for these substances, in addition to resistance by residential treatment providers to admit methadone treatment patients who might need that in-patient, more structured (as compared to out-patient) level of care for their addiction to other drugs, present barriers to potentially effective interventions.

Alcohol use also remains a problem, particularly because many patients define their difficulty in terms of illicit drug use and are resistant to the notion of giving up drinking. Given the high prevalence of hepatitis C infection in patients in methadone treatment, attention to patients' use of alcohol, which is toxic to the liver, is both a medical and an abuse-addiction problem. Accreditation guidelines and best practices documents—such as Treatment Improvement Protocol (TIP) Series 43, devised by the Center for Substance Abuse Treatment (CSAT)—draw attention to methods of dealing with these other substance use problems. Finally, nicotine dependence is highly prevalent among patients in methadone treatment, and programs are starting to develop interventions to address this problem.

TREATING OPIOID-ADDICTED PREGNANT WOMEN

Methadone maintenance has been viewed as an effective treatment for opioid addiction in pregnant women since the early 1970s. In addition to the benefits of psychosocial interventions provided by

the program, methadone maintenance treatment prevents erratic maternal opioid drug levels, thus protecting the fetus from repeated episodes of withdrawal. Programs either provide prenatal care onsite or monitor the patient to see that prenatal care is obtained elsewhere, thus reducing the incidence of obstetrical and fetal complications, reducing *in utero* growth retardation, and improving neonatal outcomes (Finnegan, 1991; Burns et al., 2006). Exposure to HIV infection through ongoing needle use is also reduced. Programs typically provide interventions focusing on nutrition, parenting skills, exercise, and other health-related topics.

Methadone-maintained mothers produce offspring more similar to drug-free controls, in contrast to the poorer health status of offspring born to women using street drugs. Methadone substantially reduces the highs and lows in maternal serum opioid levels that typically occur with the repeated use of heroin and other short-acting opioids, thereby reducing the harm to the fetus caused by repeated intoxication and withdrawal (Kaltenbach et al., 1998). Although expectant mothers can be stabilized on methadone, body changes specific to pregnancy frequently cause them to develop increasing signs and symptoms of withdrawal as the pregnancy progresses, and they may need dose increases to maintain a therapeutic plasma level and remain comfortable. Splitting the dose so that it can be ingested twice daily often produces better results, as this both reduces fetal stress and increases the comfort of the pregnant woman (CSAT, 2005).

There is inconsistent evidence to support the commonly held belief that the severity of the neonatal abstinence syndrome (central nervous system irritability, gastrointestinal dysfunction, and respiratory distress in the infant generally appearing in the newborn within the first 72 hours after birth) is proportional to the methadone dose, but many programs urge the expectant mothers to reduce their dose so the "baby won't be born addicted." In fact, the management of the neonatal abstinence syndrome is relatively straightforward—fetal discomfort can usually be eliminated within hours, and withdrawal can be accomplished within 14 to 28 days. No lasting impairment from these experiences has been demonstrated. Breast-feeding is encouraged for newly delivered mothers on methadone, regardless of their dose level, unless otherwise medically contraindicated (American Academy of Pediatrics, 2001).

ADDRESSING PSYCHOLOGICAL ISSUES

Extensive research over a long period of time has clarified the importance of the psychosocial component of methadone treatment. The stigma against heroin addicts in general, and methadone patients in particular, has created a treatment climate in which both patients and treatment providers may become demoralized about the value of these interventions. Often isolated from the mainstream, providers may not be able to obtain access to resources for patients on methadone. For example, methadone patients are often excluded from housing support (including recovery housing), mental health treatment, and vocational training programs. Nonetheless, evidence is growing that minimal intervention using methadone reduces illicit drug use (and hence needle sharing), while enhanced treatment accomplishes a great deal more (McLellan et al., 1993 and 1998).

In 1997 a National Institutes of Health (NIH) consensus panel recognized the importance of attention to medical, psychiatric, and socioeconomic issues, as well as drug counseling, in optimizing the effectiveness of methadone treatment. Psychosocial counseling focuses on managing the patient's personal problems, particularly those specific to drug use, physical health, interpersonal relationships, family interactions, and vocational and educational goals. The counselor also performs the role of the case manager and is a liaison between physicians and medical institutions, courts, and social services. Counselors help the patient to develop coping strategies for current problems, perform initial screening for medication and other program services, and attend to issues concerning program rules, privileges, and policies. The federal and state regulations and accreditation guidelines governing methadone treatment are more complex, detailed, and restrictive than others in medicine or psychology, and maintaining a therapeutic alliance while meeting these obligations is a daunting task for clinical staff.

A recent large scale epidemiologic study found that among the respondents with a twelve month substance use disorder about 20 percent had a co-occurring mood disorder with depression being predominant and about 18 percent had a co-occurring anxiety disorder (Grant et al., 2004) and depression is particularly common among the opioid-dependent population. Treatment outcome is improved by adding supplemental psychotherapy with professionally

trained staff for patients with substantial co-occurring psychiatric symptoms (Woody, 2003). It is important that such staff be well integrated into the treatment team. Psychiatric medication may also be given concurrently with methadone, and the use of antidepressants is increasingly common for methadone patients. Possible pharmacokinetic interaction effects are manageable with consistent monitoring and good staff teamwork. Psychotic conditions are less common, but clinics are likely to have some experience with highly disturbed individuals, and they should therefore be able to recognize and manage these patients appropriately. The patients benefit from the structure of frequent clinic attendance.

Twelve-step programs actively promote abstinence from all potentially addictive drugs, and this has been a barrier to the participation of methadone patients in these programs. Coupled with this are negative attitudes toward methadone and its users. The founders of Alcoholics Anonymous (AA) viewed medication interventions such as methadone as being compatible with twelve-step program participation (Zweben, 1991), but AA meeting participants may not always be open to participation by methadone patients. This climate has begun to change, however, and methadone patients are increasingly attending twelve-step meetings. Methadone maintenance programs are developing their own special meetings onsite, which in turn encourage patients' utilization of twelve-step meetings in the larger community.

HIV/AIDS AND HEPATITIS C

A positive reexamination of methadone treatment has been greatly stimulated by the documentation of its role in reducing the spread of HIV. Seroprevalence is much lower among those who have been on long-term maintenance, particularly those who entered treatment prior to the onset of the rapid spread of HIV in the local population (Batki, 1988). Research suggests that drug-use risk reduction is more likely to be achieved by those patients, both those uninfected and those infected with HIV, who remain in methadone treatment. Further, patients who drop out and return, as well as those who continue to inject while in treatment, may also benefit in this respect (Thiede et al., 2000). Clinic attendance makes large numbers of intravenous drug users accessible to efforts at prevention and education, screening, testing, and counseling. Because methadone patients have a continuing forum to discuss their life issues, counselors may be able to facilitate behavior change in relation to safer sex practices and other high-risk behaviors. Further gains accrue as the patient progresses in treatment, as an abstinent person is in a better position to exercise good judgment than an intoxicated one. Efforts are therefore being made to integrate HIV/AIDS-related activities as fully as possible into methadone treatment programs.

The hepatitis C virus (HCV) has emerged as a problem of major significance, with many clinics reporting a prevalence of up to 80 percent. Among those with HIV, co-infection with HCV is high. Inasmuch as 50 to 80 percent of new injectors become infected with HCV within 6 to 12 months, methadone maintenance will not reduce its spread as effectively as has occurred with HIV. However, it does provide a structured system in which the patient can be medically monitored, informed of emerging treatments, and educated about health practices to reduce the burden on the liver while more promising treatments are being developed. There are many complications to the provision of integrated care to these patients (Sylvestre et al., 2004).

WHAT THE FUTURE HOLDS

Methadone maintenance has demonstrated its effectiveness in reducing illicit drug use and facilitating the transition to a productive lifestyle. In the mid-to-late 1990s, two major scientific bodies, the NIH and the Institute of Medicine (IOM) reviewed the evidence on methadone maintenance and concluded that it was an effective modality whose usefulness was greatly reduced by stigma and overregulation (National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction, 1998; Rettig & Yarmolinsky, 1995). Partially in response to these two reviews, federal oversight in the United States shifted in 2001 from the Food and Drug Administration (FDA) to the Center for Substance Abuse Treatment (CSAT). That shift, accompanied by changing regulations requiring accreditation for opioid treatment programs (42 CFR Part 8), has made the service delivery system more flexible and responsive to patients' needs. Additionally, CSAT's TIP 43 provides practitioners with guidelines for best practices in methadone treatment. The release of TIP 43 was accompanied by a widespread dissemination effort

designed to increase the adoption of these practices among Opiate Treatment Programs (OTPs).

Research, including long-term follow-up studies, indicates that stabilized and socially responsible methadone patients can be safely given a month's worth of take-home medication by physicians in an office-based practice (Novick & Joseph, 1991; Novick et al., 1994). CSAT's regulations, based on that research, permit clinics to give patients up to one month's supply of medication. Take-home privileges are awarded in a step-wise fashion, with the requirements for frequency of clinic attendance decreasing over time based on the patient's progress in recovery and demonstrated responsibility in handling take-home medication.

Buprenorphine, a partial opioid agonist, has been developed and made available to opioid addicts, both in methadone clinic practice as well as from qualified physicians in office-based practice. This medication can be used for both detoxification and maintenance of opioid dependent individuals, and research seems to indicate treatment outcomes similar to methadone (Mattick et al., 2003). It is hoped that this additional medication and new treatment setting will broaden the options and possibilities for effective intervention. Federally sponsored training efforts have improved the quality of care and will continue to be essential in disseminating current information and providing opportunities for skill development. Slowly, patients have emerged as visible examples of success, and these patients are serving as positive role models for others and coming together to act as advocates for this modality. Mobile dispensing services have also been implemented. Thus, barriers to participation in residential treatment are beginning to be removed. It is hoped that these developments will engender future gains and allow methadone maintenance to gain the acceptance it so greatly deserves.

See also **Addiction: Concepts and Definitions; Hepatitis C Infection; Heroin; Injecting Drug Users and HIV; Opiates/Opioids; Opioid Complications and Withdrawal; Opioid Dependence: Course of the Disorder Over Time; Pregnancy and Drug Dependence; Rhetoric of Addiction; Treatment, Behavioral Approaches to: Twelve-Step and Disease Model Approaches; Treatment, Pharmacological Approaches to: Buprenorphine; Treatment, Pharmacological Approaches to: Methadone; U.S. Government Agencies: Center for Substance Abuse Treatment (CSAT); U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA).**

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REVISED BY T. RON JACKSON (2009)

METHAMPHETAMINE. Methamphetamine, also known as meth, speed, or crank, is an illegal psychostimulant that is abused by more than 35 million individuals worldwide; in contrast, 15 million people in the world abuse cocaine. The structure of methamphetamine is similar to that of amphetamine. Speed is abused because of its powerful stimulant properties that cause the user to experience a longer "high" than the one experienced by people who take cocaine. The drug can be taken in multiple ways, including through oral, intravenous, and smoking routes. Because it is so inexpensive to produce and to buy, users can readily gain access to it. It is eliminated more slowly from the body, and its actions can last 10 times longer than those of cocaine; this allows more time between "hits" and longer binge episodes.

Meth abuse has reached severe epidemic proportions in western, midwestern, and southern U.S. cities. Surveys have shown that about 5.2 percent of the adult U.S. population has used meth at least once, and about 6 percent of high school students have tried it. Meth-related emergency room admissions increased from 10 to 52 per 100,000 admissions between 1992 and 2002. In the past, meth

abusers were mostly truck drivers and motorcycle gang members, but more college students and young professionals are now using the drug. The greatest increase in meth use has been among men who have sex with men, because the drug is reported to boost sexual performance. Therefore, there is now a greater occurrence of meth addiction in homosexual and bisexual men than in the general population. These numbers are of concern because meth use leads to participation in high-risk sexual activities, such as frequent changes of sexual partners and involvement in unprotected intercourse.

CLINICAL TOXICOLOGY

Although meth is used because of its euphorigenic effects, the abuse of this drug is associated with serious health consequences in humans. Meth users show acute clinical signs and symptoms that include agitation, anxiety, aggressive behaviors, paranoia, hypertension, hyperthermia, cerebral vasculitis, and psychosis that resemble either manic or schizophrenic symptoms. Physicians from Japan have published papers showing that these psychotic symptoms can be long-lasting. Ingestion of large doses of the drug can cause life-threatening hyperthermia above 41°C (105.8°F), cardiac arrythmias, heart attacks, cerebrovascular accidents or strokes due to hemorrhage or vasospasm, cerebral edema, seizures, renal and liver failure, as well as death.

PSYCHIATRIC PROBLEMS OF ABUSERS

Serious concerns have also arisen over the potential chronic consequences of meth abuse. For example, neuropsychological studies utilizing a battery of tests have shown significant deficits in attention, working memory, and executive functions in chronic meth addicts. Neuroimaging studies have shown extensive damage in the brains of meth abusers. Abusers have persistent decreases in the levels of dopamine (DA) transporters in several regions of their brain. These brain regions include the orbitofrontal cortex, dorsolateral prefrontal cortex, and the caudate-putamen, which are important in daily decision making. In addition, studies done on the brains of meth abusers who died of an overdose or of other causes exhibit a 50–60 percent decrease in DA levels in the caudate-putamen. DA is the substance that is abnormal in patients who suffer from Parkinson's disease.

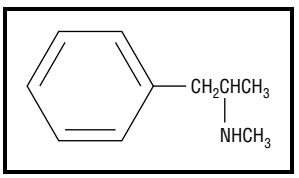

Figure 1. Chemical structure of methamphetamine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The density of serotonin (5-HT) transporters (5-HTT) is also decreased in the brains of meth abusers. This could be related to depression, from which some meth abusers suffer. Structural magnetic resonance imaging (MRI) studies in meth abusers have shown that they lose brain matter in several regions that are important for maintaining attention or making decisions. Therefore, the cognitive impairments and psychiatric symptoms observed in meth users might be related to these toxic effects of the drug on the brain.

See also **Amphetamine Epidemics, International; Designer Drugs; Epidemics of Drug Abuse in the United States.**

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JEAN LUD CADET

METHANOL. Methanol (methyl alcohol, CH_3OH) is the simplest of the alcohols. It is the natural by-product of wood distillation—an older method of producing drinking alcohol (ethanol). Chemically synthesized methanol is a common industrial solvent found in paint remover, cleansing agents, and antifreeze. It is used to denature the ethanol found in some of these solutions and thereby render them unfit for drinking.

Methanol ingestion is usually accidental, but some alcoholics resort to the desperate measure of consuming methanol when they cannot obtain beverage ethanol. Persons working in poorly ventilated areas can suffer ill effects from inhaling methanol-containing products, and ingestion of methanol is

considered a medical emergency. Methanol is metabolized to formaldehyde and formic acid by the same liver enzymes that break down ethanol (these are alcohol dehydrogenase and aldehyde dehydrogenase). The formaldehyde and formic acid are toxic metabolites responsible for the symptoms of methanol poisoning; these appear several hours or days after methanol ingestion. Blurred vision, leading to permanent bilateral blindness, is characteristic of methanol poisoning. The accumulation of formic acid results in severe metabolic acidosis, which can rapidly precipitate coma and death. Other symptoms of methanol toxicity include dizziness, headaches, cold clammy extremities, abdominal pain, vomiting, and severe back pain.

The treatment for methanol poisoning is sodium bicarbonate, given to reverse the acidosis. In more serious cases, dialysis may be required; in addition, ethanol is given intravenously because it competitively binds to alcohol dehydrogenase, thereby slowing the production of toxic metabolites and allowing unchanged methanol to be excreted in the urine.

See also **Alcohol: Chemistry and Pharmacology.**

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KAREN PARKER

METHAQUALONE. Methaqualone is a nonbarbiturate, short-acting sedative-hypnotic drug that has been used to treat insomnia. It was originally introduced in 1951 as a treatment for malaria. In the 1960s and 1970s, it became a popular drug of abuse among college students. Frequently called Quaaludes or "Ludes," the drug, like the short-acting barbiturates, produced euphoric effects; some users claimed it has aphrodisiac effects.

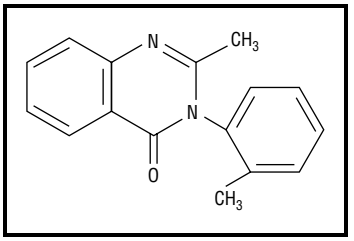

Figure 1. Chemical structure of methaqualone. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

It is usually taken in pill form, and depending on the dose, the effects last a few hours. The body eliminates about half of the ingested dose in about ten to forty hours, so that even forty-eight hours after ingestion, some drug may still be present. Prolonged use of methaqualone in high doses can lead to tolerance and physical dependence, and abrupt cessation of daily ingestion can result in withdrawal symptoms that are quite similar to those seen in barbiturate withdrawal. Fatal convulsions have resulted from sudden withdrawal. Fatal overdoses can occur when the drug is used alone, but especially when it is mixed with ethanol (alcohol) and/or barbiturates. Because it was so commonly abused in the United States, the drug was shifted to Schedule I of the Controlled Substances Act in the 1980s. Thus it can no longer be prescribed and its nonmedical use is subject to severe criminal penalties. Although methaqualone is rarely used illicitly in the United States, it is still available in other countries and is a drug of abuse in some.

See also **Addiction: Concepts and Definitions.**

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SCOTT E. LUKAS

METHEDRINE. Methedrine was the proprietary name given to methamphetamine hydrochloride by the pharmaceutical company Burroughs Wellcome.

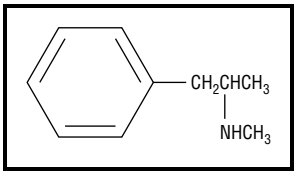

Figure 1. Chemical Structure of methedrine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

It was sold in ampules and until 1963–1964 was readily available by prescription. Methedrine (or "meth") became one of the street names of methamphetamine during the 1960s and early 1970s, when high-dose methamphetamine ("speed") was a major drug of abuse. It was a particular problem in northern California where, after the manufacturer withdrew commercially made methedrine from the market in 1963, large quantities of black-market, illicitly synthesized methamphetamine became available for sale.

See also **Amphetamine Epidemics, International; Designer Drugs; Epidemics of Drug Abuse in the United States.**

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METHYLPHENIDATE. Methylphenidate is a central nervous system stimulant, structurally related and with similar effects to amphetamine. It is used by prescription as Ritalin. It was initially marketed as a mood enhancer in the mid-1950s and described as having less abuse potential than amphetamine; however, within a few years a number of dramatic reports of its abuse and toxicity were published. Methylphenidate is commercially available (by prescription) in pill form, reaching peak effect in one to two hours. Like the amphetamines and other stimulant drugs, methylphenidate is a controlled substance, placed in Schedule II of the Controlled Substances Act to indicate that although it has medical utility, it also has substantial abuse liability.

In most people, methylphenidate increases general levels of activity, decreases food intake, produces positive subjective effects (an elevated mood), and can interfere with sleep. With continued use, tolerance can develop to these effects; users will often escalate their doses to achieve the desired effects of their initial doses of methylphenidate. Continued high-dose methylphenidate use can result in toxic consequences similar to those seen after amphetamine use—with anxiety, sleeplessness, and eventually a toxic paranoid psychosis. High-dose users often begin with oral methylphenidate use but switch to injecting the drug in order to maximize the effect and achieve the initial "rush" that is typical of intravenous drug abuse. Commercially manufactured methylphenidate pills (the only form available) contain talcum, an insoluble substance, which can cause toxic effects (such as abscesses) when the pills are dissolved in water and injected intravenously or under the skin.

Laboratory animals tested with methylphenidate show increases in locomotor activity after single doses; increased sensitivity to this effect after repeated doses; and the development of stereotyped repetitive behavior patterns after chronic dosing. In addition, these animals remain more responsive to methylphenidate even after the drug treatment has been discontinued. It has been suggested that the continuous repetition of behavior that characterizes the response to chronic methylphenidate treatment is a good model for the human stimulant psychosis. As in animals, humans who use high doses become increasingly sensitive to such stimulants as methylphenidate, with psychosis increasingly likely at lower doses after its initial appearance. There are, however, no data to support this hypothesis.

In addition to its action as an appetite suppressant, methlyphenidate has been found to have other therapeutic utility. Like *d*-amphetamine, it has been used successfully in the treatment of attention-deficit hyperactivity disorder (ADHD), a syndrome that first becomes evident during childhood and is characterized by excessive activity and difficulty in maintaining attention. Because of its relatively short half-life, two or three doses of methylphenidate are required each day, although recently a slow-release form of the medication has become available, promising more stable blood

levels with only a single daily dosing. Methylphenidate has been shown to alleviate or moderate many of the symptoms of this disorder, although it is not effective in all cases and its long-term efficacy is not well understood.

Side effects of treatment can include insomnia, loss of appetite, and weight loss, all effects of stimulant drugs in general. In addition, concern about the longer-lasting effects on learning and cognition in youngsters maintained on this drug for many years has made practitioners cautious and often unwilling to prescribe it. Recent research and practice, however, has supported methylphenidate as the stimulant of choice for treating this disorder. As with the amphetamines, methylphenidate is also effective in the treatment of narcolepsy, in which sudden attacks of sleep can occur unexpectedly.

See also **Amphetamine; Anxiety; Attention Deficit Hyperactivity Disorder.**

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MARIAN W. FISCHMAN

MEXICO. The following text will discuss different issues of the addictive substances in Mexico, with a special focus in psychoactive drugs: the evolution of the trends in their consumption; the changes in official perceptions of drugs; the organized crime dimension of the problem; some of the policies that the Mexican government has developed to confront the drug trafficking; and the general perspective of the bilateral relation of Mexico and the United States on the topic.

THE ILLICIT DRUG TRADE

A number of different plants that are used to produce psychoactive substances and drugs have long been a natural part of the Mexican landscape. In the fields of some states, including Oaxaca, Guerrero, Michoacán, Sinaloa, Durango, and Chihuahua, the marijuana plant (*Cannabis sativa*) grows naturally, while some states, such as Guerrero, Sinaloa, and Durango, have been fertile ground for the opium poppy (*Papaver somniferum*). Such other states as San Luis Potosí, Chihuahua, Oaxaca, and some others in the central region, are native soil for a variety of hallucinogenic plants, principally the peyote cactus (*Lophophora williamsii*), which contains the psychoactive substance mescaline.

In Sinaloa, for example, one of the emblematic states of modern drug production in Mexico, statistical data show that the opium poppy and marijuana plant were part of the local flora in 1886. In the nineteenth century, it was not illegal to grow, possess, use, or sell such plants; in addition they had a number of legal uses, including medical and industrial purposes.

In the early twentieth century, however, the Mexican government began to legislate the use of these plants and substances. Despite these early prohibitions, the plants continued to be harvested for illegal use. Since that time all these states have been affected by the increasing development of illegal organizations seeking to profit from the illicit drug business.

By 1926 there were several cultivated poppy fields in Sonora in northwestern Mexico. The opium produced there went to the Chinese community in Mexico and to the U.S. market. The smoking of opium was associated with Chinese communities, and it fostered racist attitudes and actions against the Chinese. There were even policies of segregation in some northern states, such as Sinaloa and Sonora, at this time.

The expansion of the illegal export of illicit substances strained U.S.-Mexico relations. By 1947 the U.S. Federal Bureau of Narcotics estimated that Mexican poppies covered 4,000 to 5,000 hectares (10,000 to 12,500 acres), yielding between 32 and 40 metric tons of opium, at least half of which was turned into morphine or heroin. Mexican brown heroin became an increasingly important staple in the U.S. market, where it served as a substitute for white heroin from the Middle East and Far East from the 1950s through the 1970s.

Beginning in the 1970s, Mexico also became an important bridge for South American drugs such as cocaine (methylbenzoyl ecgonine) and white heroin, a purer version of the brown heroin processed in Mexico. These drugs are generally smuggled into Mexican territory from Colombia and Peru. In addition, from the 1990s through the first decade of the twenty-first century, such synthetic drugs as methamphetamine were increasingly being produced in clandestine laboratories in Mexico.

THE CONSUMPTION OF ILLICIT AND LICIT ADDICTIVE SUBSTANCES

According to Astorga (2005, pp. 17–24), between 1888 and 1911 the importation of opium to Mexico ranged from 800 kilograms (about 1,600 pounds) to around 12 tons. Although the opium poppy was part of the flora of Mexico, the chemical process to turn it into drugs was developed and used mostly by pharmaceutical laboratories of more industrialized countries. The product usually came from Europe and the United States; and the use of opium derivates, for medical purposes, was legal and accepted. In the eighteenth century, curative properties were attributed to such substances as cocaine (which was diluted in wine) and marijuana (which was purported to heal asthma), and they were sold legally. Until the 1930s, it was not unusual for such substances to be considered curative, and they were advertised as such throughout the country.

There is no evidence of serious problems of addiction within the Mexican population during the eighteenth and nineteenth centuries, and even up to the second third of the twentieth century. This is partly because recreational drug use was not common, while medical usage generally encouraged a controlled pattern of consumption as recommended by healthcare practitioners and the pharmaceutical laboratories (Astorga 2005, p. 24). In fact, up until the last third of the twentieth century the recreational use of such drugs was not socially supported. Even in the areas where marijuana and amapola (poppies) were grown, there was an implicit cultural framework that allowed men to drink alcohol in large quantities as a way to show their manhood but discouraged the use of drugs because it was considered a sign of a weak spirit.

However, these patterns of consumption have changed to a certain degree, and the use of these drugs has increased consistently since the 1980s, especially in some urban zones. For example, between 1988 and 1998, the consumption of marijuana in males between thirty-five and sixty-five years of age increased from 3.6 percent to 9.8 percent. Among the same population, cocaine use grew from 0.4 percent to 2.1 percent. Heroin usage also grew from 0.01 percent to 0.3 percent, but its consumption is still considered marginal. A survey of Observatorio Epidemiológico de las Drogas (Epidemiologic Observatory of Drugs), published in 2001, revealed that only 1 percent of the population had used marijuana more than fifty times in their lives, while 0.3 percent had used cocaine in this quantity, and only 0.1 percent had consumed this much heroin.

Data from the 2002 *Encuesta Nacional de Adicciones* (National Survey of Addictions) revealed that 3,508,641 persons in Mexico had used illicit drugs at some point in their lives. Data from the Consejo Nacional de Población (National Council of Population) establishes that in 2002, the population of Mexico approximated 103 million people.

Of this universe of consumers, 1,182,345 had used drugs more than six times in their lives. The most commonly used drug was marijuana and the second was cocaine. The utilization of heroin was marginal, however. This preference in consumption was consistent between the early 1990s and 2002.

Information from 2001 established that drug consumption was highest in the city of Tijuana, where 6.7 percent of the population had used drugs at some point in their lives, followed by Ciudad Juárez (5 percent), Ciudad de Mexico (3.3 percent), Guadalajara (2.2 percent, which is the national average), Monterrey (1 percent), and Matamoros (0.9 percent).

The National Survey of Addictions (2002) reveals that licit addictive substances clearly have a wider use than illicit substances in Mexico, as they do elsewhere. In 2002, it was reported that more than 16,371,601 people in the country smoked tobacco, and 1,009,128 of them were considered to be dependent on it. At the same time 7,639,874 consumed cigarettes on a daily basis but did not show symptoms of dependency. Of the total population of smokers, 71.8 percent were older than 35 years of age; 25.7 percent were between 18 and

34 years old; and 2.5 percent were legally under age for smoking tobacco.

Alcohol has also been a frequently used substance in Mexican culture, and it has had a tradition of wider social acceptance than psychoactive substances and illicit drugs. In 2002 the number of people who had consumed alcohol at least once during their lifetime was 32,315,760. Of these, 4,914,166 reported that they drank from one to four times a week, while 947,099 declared that they consumed alcohol almost daily.

Official consumption surveys have been a useful tool in evaluating drug trends among the Mexican population. The methodology used is believed to be accurate and is generally compatible with international standards. However, one of the concerns that has arisen is the long delay in the disclosure of the data. The 2002 National Survey of Addictions was still the most recent source of information in 2008 because the 2004 survey had not yet been released. This delay presents obvious difficulties in evaluating consumption trends, making it extremely difficult to determine if the use of drugs is becoming a greater or lesser problem within the Mexican population.

DRUG CONTROL AND THE EVOLUTION OF THE PROBLEM

Mexico's international drug-control efforts began with the Shanghai Convention of 1909 and the Hague Opium Convention of 1911–1912. Drugs were proscribed through different legal measures during the first third of the twentieth century. In 1920 the Mexican government forbade the growing of marijuana and restricted the cultivation of poppies. In 1923 Mexico's president, Álvaro Obregón, prohibited the production of opium. By the early 1920s the Mexican press had begun to publish reports of isolated violent crimes committed by intoxicated people. The statistical data, however, do not support an assessment that drugs were causing higher levels of violence at this time. While this was a relatively violent period in Mexican history, the causes of this violence were mainly due to the aftereffects of the Mexican Civil War (1910–1920).

During this period, Mexican authorities agreed to cooperate with international efforts to reduce the supply of illicit psychoactive drugs, particularly measures aimed at poppy and marijuana cultivation. This was more a gesture of good will to international cooperation than a strong effort to solve an unperceived problem for the country. In 1934, President Lázaro Cárdenas del Río created the government's first centralized narcotics unit. Because drugs were considered a public health problem rather than a criminal problem, the unit was put under the direction of the secretary of health.

Mexico gradually moved toward a more restrictive policy against narcotics, including the use of law enforcement agencies, but it was not until the late 1990s that the effects of crime rings and violence related to drugs became a real concern. Despite official speeches by high-ranking public servants, the perspective of the Mexican government and the public was that Mexico merely served as a "bridge" for foreign drugs on their way to the big market in the north. The customary public discourse was to blame the demand for drugs in the United States for all the undesirable issues related to drugs in Mexico.

OPERATION CONDOR AND CORRUPTION

It was not until 1975 that the Mexican federal government developed a more concerted effort to eradicate the illicit cultivation of psychoactive plants. This effort, known as "Operation Condor," included the deployment of 10,000 troops in the rural areas of the most affected states (Sinaloa, Durango, and Chihuahua), as well as enforcement operations by the Dirección Federal de Seguridad (Federal Security Directorate, or DFS) in the cities. The origins of this effort can be traced to American public concern about drug shipments that were smuggled through the Mexican frontier. U.S. pressures had led to the virtual closure of the border in the San Ysidro area for three weeks in 1969, and the Mexican government eventually felt the need to take stronger actions.

The campaign produced some results in the short term, but it certainly did not eradicate the drug problem in Mexico. Unfortunately, the operation led to a dramatic increase in human rights abuses and to higher levels of corruption in the federal agencies, especially the DFS. Some of this agency's chief commanders became protectors of criminal groups, and some became drug traffickers themselves. The involvement of several DFS commanders in the protection of drug-trafficking operations was uncovered after Enrique Camarena,

an agent of the U.S. Drug Enforcement Agency (DEA), was kidnapped, tortured, and murdered in 1985. The murder was plotted by Rafael Caro Quintero, a member of the ring of Miguel Angel Félix Gallardo, and owner of Rancho "El Búfalo," in Chihuahua, where in November 1984 a massive quantity of marijuana (between 5,000 and 10,000 tons) was discovered under the custody of DFS agents. Camarena's murder was assumed to be a retaliation for the seizure of El Búfalo. The high level of corruption within DFS was clear when Caro Quintero was arrested after Camarena's murder: he had an official identification as a DFS member, signed by his General Director, Antonio Zorrilla Pérez. The level of corruption became so untenable at this point that the DFS was dissolved.

The murder of Camarena focused public attention on the decreasing effectiveness of Mexican drug-control efforts and the pervasive corruption that had eroded Mexican security institutions. It was also a turning point in U.S.-Mexico relations. Drugs became a confrontational issue at uncharacteristically high levels of the two governments. Both the U.S. secretary of state and Mexico's foreign minister spoke of the murder (and the subsequent government response) as a paramount diplomatic issue. From this point forward, drug control would no longer be treated only as a law-enforcement issue. In response to continuing U.S. pressure, the Mexican government took a series of actions that resulted in the apprehension and incarceration of several drug traffickers. Nevertheless, trafficking and corruption increased, and tensions between the two governments remained high throughout the 1990s.

In the mid-1970s and early 1980s, the traffic in cocaine also increased in Mexico. The United States strengthened its patrols along the shores of Miami, which pushed the already dominant Colombian cartels to seek out different routes for their illegal product. This development then fostered contacts between Mexican and Colombian traffickers. Up until this time, the Mexican drug rings dealt only with marijuana and lower-quality heroin, but this new relationship with the Colombians allowed them to trade in cocaine, a drug that was more in demand and more profitable.

At the beginning of this alliance, the Colombian cartels used their Mexican partners merely to carry their product; but different local conditions, the presence of Mexican criminal networks that had already commercialized other drugs, and the often necessary passage through Mexican territory to reach the U.S. market led to a larger role for the Mexican cartels. In the first decade of the twenty-first century, U.S. authorities estimated that around 80 percent of the cocaine that reached American territory was coming through Mexico and being transported by Mexican criminal organizations.

The Mexican cartels further strengthened their power during the 1990s, and the corruption problems within the government agencies remained. Even higher Mexican officials were prosecuted for protecting criminal organizations, including Jesús Gutiérrez Rebollo, the director of the National Institute to Combat Drugs (INCD), who was arrested on corruption charges in 1997. He was condemned by Mexican courts for crimes against health (*delitos contra la salud*), organized crime (*delincuencia organizada*) and bribery (cohecho). He has been in a high security prison at Almoloya de Juárez, Estado de México since the year of his arrest.

Several authoritarian features of the Mexican political regime of this period, which was marked by decades of one-party rule, actually encouraged the drug business. There were high levels of impunity within the government and a gradual loss of control of the different security institutions, leading to a weak rule of law, poor accountability, and a strongly rooted belief in the private use of public resources. The administration of President Ernesto Zedillo (1994–2000) dealt a blow to the corrupt political structure that protected drug-trafficking operations, but it could not dismantle it completely. In 1997 the level of cooperation between Mexico and the United States was improved through the establishment of the United States-Mexico Bi-National Drug Strategy, which was an effort to create a more integrated effort to confront the drug problem.

A NEW PRESIDENT AND RENEWED HOPE

The 2000 election of Vicente Fox as president marked the end of seventy-one years of rule by the Institutional Revolutionary Party (PRI). Along with renewed hopes for a democratic revival, there were expectations of a dramatic change in the fight against drug trafficking and corruption. The Fox

administration (2000–2006) was able to bring some important kingpins to justice but lacked an internal strategy to confront the criminal organizations, and did not continue its predecessors fight against high-level corruption. Several of these groups were thus able to maintain or even increase their operations. Ironically, as these criminal organizations grew stronger, they found they were no longer hemmed in by the corrupt schemes of the old regime. As in many corrupt systems, various mechanisms of control had been established by the police and other government agencies, and these had served to constrain the criminal enterprises to some extent. Corruption remained embedded in local institutions; neither did it completely disappear from the federal government.

The most powerful drug organizations in Mexico in 2006 were the Sinaloa Cartel, directed by Joquín "el Chapo" Guzmán Loera; the Gulf Cartel, which was led by Osiel Cárdenas until he was extradited to the United States in 2007; the Juárez Cartel, of the Carrillo Fuentes family and whose former leader, Amado Carrillo-Fuentes, died in 1997; the Tijuana Cartel, also known as the Arellano-Felix Cartel; the Millenium Cartel, led by Armando and Luis Valencia; the Amezcua-Contreras organization; and the Díaz Parada Cartel, whose leader, Pedro Díaz Parada, was arrested in January of 2007.

The pervasive corruption in local public power matched the interest of unleashed criminal groups in escaping the constraints placed on them by the old mechanisms of control that Federal police exerted. Under the Fox administration, criminal organizations sought to expand their areas of influence and control strategic places from which to export drugs to the American market. They also increased their ability to sell drugs in Mexico itself. A weakened federal capacity to impose the rule of law (or even the old clandestine agreements), the lack of political will to fight corruption that protected the criminal organizations, and the ambitions of criminal organizations resulted in previously unseen levels of drug-related violence. There is no official account of the homicides linked to the struggles of the cartels during this period; but prestigious press publications, such as *Reforma Daily*, have estimated that more than 12,000 people were killed between 2000 and 2007.

In the last third of his administration, Vicente Fox developed a program called *México Seguro* (Operation Secure Mexico), which was designed to reduce this violence. It consisted principally of the federal forces patrolling the streets of some cities and the establishment of checkpoints along certain highways. The results were poor, however, even though Mexican eradication efforts had improved since the mid-1990s. President Felipe Calderón, who took office on December 1, 2006, has shown an especial interest in fighting Mexican drug-trafficking organizations, and his government has deployed military forces in the states that have been most affected by drug-related violence. His administration has also been open to wider international cooperation, especially with the United States. For example, some of the important drug kingpins that were in Mexican prisons were extradited to the United States at the beginning of Calderón's tenure. The government has also set up a support plan, called *Iniciativa Mérida*, which will distribute material resources from the U.S. government—US $1.5 billion distributed over three years—in order to reinforce Mexican capabilities against drug organizations. The violence continues, however, and it is not clear that the new strategy will be effective in controlling the drug problem. Many feel that the policy lacks a core component necessary for it to succeed. They feel that the lack of a strategy to fight the corruption, which has been the central factor eroding the nation's capacity to control violence and drugs, dooms the policy to failure.

See also **Bolivia; Colombia; Drug Interdiction; International Drug Supply Systems.**

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MICHIGAN ALCOHOLISM SCREENING TEST (MAST). The Michigan Alcoholism Screening Test (MAST) is a brief self-report questionnaire designed to detect alcoholism (Selzer 1971). The twenty-four items were designed to provide a consistent, quantifiable structured interview that could be rapidly administered by nonprofessional as well as professional personnel. Although it was once used widely in clinical and research settings, it has since been supplanted by such other screening tests as the Alcohol Use Disorders Identification Test. The twenty-four scored items assess symptoms and consequences of alcohol abuse, such as guilt about drinking; blackouts; delirium tremens; loss of control; family, social, employment, and legal problems following drinking bouts; and help-seeking behaviors, such as attending Alcoholics Anonymous meetings or entering a hospital because of drinking. Symptoms included in the MAST are not explicitly linked to any standard diagnostic system, such as the criteria for alcohol dependence in *DSM-IV* or *ICD-10*. Rather, the items were derived from the author's clinical experience or borrowed from epidemiological surveys of alcoholism and problem drinking conducted in the 1960s.

To complete the MAST, individuals answer yes or no to each item. The items are weighted on a scale of 1 to 5, depending on the assumed severity of the symptom. For example, items concerning prior alcohol-related treatment experiences and help-seeking behaviors receive higher weights. The total MAST score (range: 0–53) is derived by adding the weighted scores from all items that are endorsed. Studies indicate that the long version of the MAST possesses good internal-consistency reliability, as indicated by Cronbach's alpha coefficients of .83 to .93 (Gibbs 1983). This result suggests that the scale measures a unitary disorder.

Selzer (1971) originally recommended adopting a cutting score of 5 or higher for a diagnosis of alcoholism with the MAST. However, since this cutting score produced a relatively high percentage of false positives (Gibbs 1983), Selzer, Vinokur, and van Rooijen (1975) suggested the following cut points: 0 to 4, absence of alcoholism; 5 to 6, possible alcoholism; 7 or more, probable alcoholism. Skinner (1982) recommended that scores of 7 to 24 be regarded as clear evidence of alcohol problems, and that scores of over 25 be considered evidence of substantial alcohol problems. Ross, Gavin, and Skinner (1990) compared scores on the MAST to diagnoses of alcoholism obtained from the National Institute of Mental Health Diagnostic Interview Schedule (NIMH-DIS) (Robins, et al. 1981). A score of 13 or greater yielded the highest overall classification accuracy.

Several shorter versions of the MAST have been developed, including the thirteen-item Short-MAST (SMAST) (Selzer, et al. 1975) and the ten-item Brief-MAST (Pokorny, et al. 1972). The validity of

the MAST has been examined in a number of studies in which MAST scores, or scores from the shorter versions of the instrument, were compared to other measures of drinking status, including diagnostic interviews, physicians' diagnoses, and other self-report instruments. In reviewing twelve of these studies, Gibbs (1983) concluded that MAST diagnoses agreed with diagnoses of alcoholism reached through other assessment procedures in about 75 percent of cases. Where inconsistencies between results were found, the MAST tended to overdiagnose alcoholism. This finding probably reflects the fact that a cutting score of 5 or higher on the MAST was used in these studies. By adopting a cutting score of 13, Ross and colleagues (1990) were able to achieve a greater degree of agreement when comparing MAST scores to DIS-derived diagnoses.

As with any instrument that relies on the veracity of self-report information, the reliability and validity of the MAST are dependent on the willingness of the interviewee to answer the items truthfully. All the items possess high face validity, which means it is relatively easy to answer so as to appear non-alcoholic. The MAST may, therefore, not be a useful screening tool with individuals who are motivated to conceal their alcohol problems.

See also **Addiction Severity Index (ASI); Diagnosis of Substance Use Disorders: Diagnostic Criteria; Diagnostic and Statistical Manual (DSM); Minnesota Multiphasic Personality Inventory (MMPI); Models of Alcoholism and Drug Abuse.**

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MIDDLE EAST. Persia was one of the first regions to cultivate and consume wine. Jars found in the Zagros Mountains dating from 5400 to 5000 BCE. contain remnants of wine. Writings found at Persepolis highlight the extensive wine consumption at Persian banquets. The Greek philosopher Herodotus commented on the abundance of wine in Persia and its extensive use during feasts.

WINE

Within pre-Islamic Zoroastrianism, wine symbolized liquid gold and the fire of the sun. Drinking wine at dawn represented the joining together of the new moon and the sun. When the ruler (*sahibqiran*) drank wine, he brought the two together becoming the *master of conjunction*, the title of the Shah.

Islamic prohibitions against the use of alcohol never eradicated its use. Sufis and other sects such as Qalanders defied religious orthodoxy with their open consumption of alcohol. Persian poetry from the Islamic era, in fact, contains positive wine imagery celebrating Dionysian excess.

The Mongols, who dominated vast areas of the Middle East in the thirteenth century, both drank and were licentious. The Mongol taste for alcohol shifted from fermented mare's milk to stronger varieties when they conquered Persia. Brothels and taverns flourished under Mongol rule (1295–1304) within Persia. This culture of excessive alcohol consumption affected the early Ottoman sultans Bayazid I (1389–1402), as well as Timur Lang, the central Asian warlord, and Sultan Babur (1483–1530), founder of the Indian Mughals.

When the Christian territories of Georgia and Armenia both fell under Persian suzerainty, large numbers of enslaved males were forced into the

elite Ghulam military caste. Nominally converting to Islam, they brought their wine-making skills into elite Safavid Persian society.

The Persian town of Shiraz became famous for its red and white wine brewed by Armenian and Jewish minorities. Shiraz wine was reserved specifically for the Shah. Iranian rulers generally only consumed Persian wine and abhorred the alcoholic gifts presented by Europeans. The poor did not consume alcohol because it was reserved for the elites. The decisive defeat at the battle of Chaldiran in 1514 by the Ottoman Turks was perceived to have been caused by inebriated commanders.

The Safavid rulers initiated periodic edicts banning alcohol for various reasons: for atonement, to display leadership strength, due to a pious vizier's influence, because of adverse economic conditions, due to the need to raise taxes from a minority, for scapegoating, or as a result of health advice provided by a physician. Essentially these edicts were attempts to set limits on public behavior, but they never affected choices within private spaces. Therefore, what happened in people's homes was left to the residents, and alcohol consumption was never eradicated. The royal cellars were locked, for example, but their contents were never destroyed.

With the development of distilled liquors in the West, the elite tastes in the Ottoman and Qajar dynasties changed to rum, vodka, and champagne. Concurrent with the increase in consumption of distilled liquors, there was a decline in religious observance in the latter part of the nineteenth century and a growing belief in Sufism. The general open disregard for religious observance and the adoption of English and French cultural tastes outraged the religious orthodoxy.

TOBACCO

The English began to use tobacco extensively around 1580. Persia and the Middle East were introduced to tobacco by Portuguese sailors around 1590. By 1620 the German traveler Heinrich von Poser noted the extensive use of tobacco in Qandahar. The English originally imported tobacco to the region, although its strong flavor and cost allowed the Indian variety with its milder taste and affordability to capture the market.

In the 1650s tobacco imports dwindled as the Persians cultivated the plant. By 1700 Persia was exporting tobacco to the Ottoman Empire and Russia. The main form of inhalation was performed via a water pipe and the Iranian varieties were grown specifically for this market. The use of tobacco grew among the poor, the military, and the social elite. People differentiated their social status by the tobacco ritual and the implements they used. The poor used the base of a coconut or a gourd and the rich had jewel-encrusted crystal pipes, known as *qalyan*.

OPIUM

Opium was used throughout ancient Middle Eastern civilizations. Sumerians, Assyrians, Babylonians, and Egyptians, all describe its use in their earliest recorded histories. Grown extensively in Asia Minor and in Mesopotamia, it was traded among the Greeks, Jews, Persians, and Carthaginians. Part of an international currency, opium was used for various ancient economies among people involved in trade, slavery, travel, and war.

The evidence for widespread opium use in the Middle East is derived from a number of historical sources. The Roman writer Prosper Alpinus stated Egyptian opium was consumed in the form of *cretic wine opium*, a wine flavored with spices. The Egyptian town Sicyon became known to the Greeks as Mekone, a Greek work for poppy, so named for its extensive opium cultivation. The *Ebers Papyrus,* dating from 1500 BCE, describes an Egyptian opium mixture used to put children to sleep and stop them from crying. Homer (ninth century BCE) mentions opium in his epics *Iliad* and *Odyssey* as being used by warriors. Nepenthes (from a Greek word meaning "grief or sorrow") fortified with opiates became the drink of forgetfulness, used by Greek warriors before battle to dull their fears. The Greek god of sleep Hypnos is depicted as pouring poppy juice over his eyelids to assist his descent into sleep. Opium-laced electuaries (from a Greek word meaning "to lick up", medicinal mixtures made with jam or honey) were also used within the ancient world to prolong and enhance sexual performance. In Jewish history bronze coins of John Hyrcanus, prince and high-priest of the race of the Maccabees (135–106 BCE), portray the poppy plant. Hebrews called it *ophion*; Arabs, *af-yun*; the Chinese, *o-fuyung*; and the Greeks, *opion*.

After the Islamic conquest of the ancient world, Arab physicians drew on this ancient knowledge.

Opium was used to cure diarrhea. Avicenna (CE 980–1037, Abū 'Alī al-Husayn ibn Sina) described opium as the most powerful of the soporifics in *The Canon of Medicine*. This classic text, which was translated into Latin in 1175, became the standard medical textbook until the seventeenth century. The noted Ottoman physician Serafeddin Sabuncuoglu used opium in the fourteenth century to treat headaches, migraines, and other ailments as noted in his *Surgical Atlas*.

Opium was apparently brought to China and other parts of the eastern world in the ninth century by Arab traders. In 1511, while he was in India, Duarte Barbosa described opium as an Indian product in his description of the Malabar Coast. In 1546, French naturalist Pierre Belon traveled through Asia Minor and Egypt and found its extensive use among Turkish people, who were impoverished by their addiction.

In Persia during the Safavid period (1501–1722), opium was used by all social classes. It was more easily obtained than alcohol and had less religious strictures placed upon its use. Although widespread among the intelligentsia it was also extensively used by the poor. Opium was cheap, suppressed the appetite, and alleviated misery. It was also used by soldiers to boost strength, administered as a medicine, and used by libertines to prolong sexual satisfaction.

Although subject to ban in the Qajar period (1794–1906), in 1796 the population ignored the ban. Opium, though ingested widely in the Persian Empire, was consumed within limits. Women and men used the drug as a panacea for the rigors of aging, to fortify the body and the spirit against the loss of physical strength.

In the 1880s there was a gradual switch from opium eating to opium smoking. Drug use became a paramount preoccupation. The change arose from the introduction of smokable forms of opium from China.

Iran's increasing use of opium was supported by internal production. As an example, in 1859, around 42,000 pounds of opium were grown. By 1926, the amount had increased to one million pounds. Initially Iranian merchants tried to export opium to China thereby undercutting the British trade. The British responded by imposing high tariffs, which made the trade expensive and led to adulteration of the drug to boost profits. Chinese dissatisfaction caused the trade to dwindle in the late nineteenth century. However, Iranian peasants switched from growing cereals to poppy cultivation, and new markets opened as Iranian opium became the major export crop. The effect on the home market was extensive. In 1910 opium smoking was banned, although the population could still consume it. In 1928 a taxation system was introduced to limit production and consumption.

In 1936 Iran was producing 1,350 tons of opium, one of the largest supplies in the world, earning the country 15 percent of its foreign exchange. Iran's drug using population was second only to China by 1949, with an estimated 1.3 million people addicted, one in nine of the population. Iran exported opium to the Allies and the Axis Powers during World War II. Iran's great families had become rich from the opium trade, including the Pahlevi family, the ruling dynasty that owned numerous opium fields. In 1943 following the Third Millspaugh mission, the United States took over the Iranian economy, which involved overseeing the opium production. Iranian opium was sent to Kachin soldiers in Burma by the United States.

Between 1951 and 1953 Prime Minister Mohammed Mossadegh (1882–1967) of Iran banned opium consumption and production. His government also nationalized oil firms, which resulted in Operation Ajax, a coup organized by the British and American Secret Services. During the ban the estimated number of addicts fell to 350,000. Production shifted to Turkey and Afghanistan, which produced opium and heroin for Iranians. The ban in Iran lasted nominally for 14 years, but U.S. antinarcotic sources noted the ban did not apply to the ruling family who returned to power with U.S. and British support. Iran bordered the U.S.S.R. and was a bulwark against Soviet expansion into the oilfields of the Middle East. Following the toppling of Mossadegh, heroin use continued to escalate.

The Iranian revolution of 1979 created a seismic shift in Middle Eastern politics, producing the first nonaligned Muslim state following the abdication of the shah. Smokable forms of heroin were introduced in the United Kingdom by Iranian refugees fleeing the revolution.

Any nominal limits placed upon the internal opium trade by the previous regime disintegrated. Ayatollah Khomeini (1902–1989), although denouncing drug dealers as traitors, concentrated on banning alcohol. Despite the Western perception that the regime had complete authoritarian control, drug use significantly increased with an estimated 2 million people addicted. With the explosion in drug use, Iranian drug cultivation expanded to meet the new demand. This meant the Afghan/Pakistan heroin production could no longer penetrate this particular market and had to find other trade routes.

OPIUM AND WAR IN THE MIDDLE EAST (AFGHANISTAN, LEBANON, AND IRAQ)

The war in Afghanistan against the Soviets from 1978 until 1989 allowed Afghan heroin to find a new supply route onto the streets of Berlin, Amsterdam, Milan, and London rather than into the streets of Tehran. It was through this burgeoning opium trade the *mujaheddin* (holy warriors) were able to finance their war of liberation and establish a Muslim state. The mujaheddin were assisted by Western security forces that financed Hekmatyar, an Afghani heroin warlord. The Afghani heroin trade expanded in response to the 1979 Soviet invasion, destabilizing the region.

The United States had maintained a constant presence in Lebanon following World War II. There, the U.S. provided support for the Christian Maronite community, who were involved extensively in the growth and distribution of Lebanese cannabis. In 1958 the CIA assisted the Christian Maronites in gaining political power by becoming involved in elections in Lebanon. Subsequently, there were questions regarding the legitimacy of the election results and the CIA's role in the political process.

During the Lebanese Civil War (1975–1990) Lebanon's Beqaa Valley became a major center of opium and cannabis production, which helped the militias purchase weapons. The Beqaa is situated 30 kilometers (19 miles) east of Beirut between Mount Lebanon to the west and the Anti-Lebanon mountain ranges to the east.

In the time of the Roman Empire, the Beqaa Valley was a major supplier of grain to the Levant. In the early twenty-first century, the area represents 40 percent of Lebanon's arable land. The valley produces hashish and cultivates opium poppies along with other produce. U.S. pressure on Syria, the occupying force, brought about the eradication of cannabis and opium poppies after the civil war ended. One unintended consequence of the U.S. eradication program was the switch by the Lebanese narcotics producers to importing morphine base from Afghanistan/Southeast Asia and coca base from South America. These narcotics were refined into heroin, cocaine, and crack in chemical laboratories in the Beqaa Valley and then exported.

The Hezbollah conflict with Israel in 2006 saw the reseeding of plants as governance in the area disintegrated. The UN also reneged on promises made to the farmers, who had been enticed to give up production in return for alternative crop subsidies, new electric power stations and irrigation projects. As of 2008, Hezbollah controls much of the Beqaa Valley. Officially Hezbollah is opposed to narcotics but cannot risk armed confrontation with the powerful Beqaa Valley clans.

The U.S.-led invasion of Iraq in 2003 entailed a shift to growing locally produced opium, sold by the various militia vying to fill the vacuum following the ousting of the Ba'ath Party. Heroin and opium use within Iraq expanded as a result of the fighting following the occupation. There has been an expansion of opium poppy cultivation and a marked increase in heroin use by Iraqi youth.

See also **Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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DEAN WHITTINGTON

MILITARY, DRUG AND ALCOHOL ABUSE IN THE UNITED STATES.

The United States military has been associated with substance use in various contexts from the inclusion of rum in daily rations prior to the 1830s (Musto, 2002), to free cigarettes being made available to troops during both world wars (Sloan, Smith, & Taylor, 2002; Tate, 1999) and to the use of narcotics during the Vietnam War (Robins, 1993). A better understanding of substance use in the military, however, must begin with a more general discussion of drug use in the civilian population.

DRUG AND ALCOHOL ABUSE IN THE UNITED STATES

In 2004 Sarah W. Tracy and Caroline Jean Acker averred that the use of consciousness-altering substances has a long history in the United States. Included in this history is the legal status of substances. For example, Griffith Edwards (2004) discussed the criminalization of drugs such as opiates and cocaine that began in the early 1900s with the Harrison Act and the prohibition of cannabis, which began in the 1930s with the Marijuana Tax Act, in his book *Matters of Substance, Drugs—and Why Everyone's a User*. In his 2004 book, *Altering American Consciousness: The History of Alcohol and Drug Use in the United States, 1800–2000*, Ron Roizen asserted that alcohol, briefly prohibited legally during the 1920s, was subject to a "relative tightening in drinking norms" (p. 69) during the 1980s that may have co-occurred with a reduction in use. Tobacco, although still legal, is the target of both scientific research as reviewed in a 2004 report of the surgeon general issued by the U.S. Department of Health and Human Services, and social movements against the substance as explored by Mark Wolfson in 2001.

Results of the 2006 National Survey on Drug Use and Health (NSDUH) illuminate differences in rates of use between illicit and licit substances. Illicit drug use, with marijuana being the most commonly used drug, was reported among the civilian population of the United States, aged 12 or older, at a rate of 8.3 percent in 2006. These statistics provided by the Substance Abuse and Mental Health Services Administration in 2007 also showed that the nonmedical use of prescription-type psychotherapeutic drugs exceeded that of cocaine, hallucinogens, and methamphetamine. Inhalant use was at 1.8 percent. In contrast, 23 percent of persons aged 12 or older reported binge drinking, defined as five or more drinks on the same occasion at least one day in the preceding month. Additionally, 6.9 percent of persons over the age of 12 reported participation in heavy drinking, defined as binge drinking at least five days in the preceding month. The rate for adults aged 18 to 25 was higher at 15.6 percent. A quarter of the population reported current cigarette smoking.

DRUG AND ALCOHOL ABUSE IN THE MILITARY

In their 2007 article, Robert M. Bray and Laurel L. Hourani describe how the Department of Defense (DoD) has collected comprehensive data regarding substance use and other health behaviors among military personnel using the Worldwide Survey of Alcohol and Nonmedical Drug Use since 1980. According to a comparison in 1991 by Bray, Mary Ellen Marsden, and Michael R. Peterson of the 1985 DoD survey and the 1985 National Household Survey, which was standardized with regard to age, race, education, and sex, illicit drug use among military personnel was lower than drug use in the civilian population. In 2007 Bray and Hourani reported that the rate of illicit drug use started dropping after the initial DoD survey series in 1980 and began to level off in 1992. Between 1998 and 2002, rates of illicit drug use remained relatively unchanged. Bray and others (2006) showed that in 2005 the standardized rate of illicit drug use for military personnel was still lower than that of civilians. Illicit drug use among military personnel in 2005 was not comparable to previous years due to a change in the wording of questions.

For alcohol use, the picture is much different. In 1985 both male and female military personnel between the ages of 18 and 25 were more likely to report drinking any alcohol than were civilians, according to Bray et al. (1991). Military men between the ages of 18 and 55 reported more heavy drinking than civilian men. A study published in 2007 by Katy L. Benjamin, Nicole S. Bell, and Ilyssa E. Hollander comparing alcohol-related hospitalization rates from 1980 to 1995 found that although both groups demonstrated increases in rates that eventually resolved to earlier levels, the army increases began earlier, rose higher, and lasted

longer. Army rates began to increase in 1984 and returned to earlier levels by 1991. The authors of this study hypothesized that this may have been due to a "substitution effect," the result of 1984 DoD mandatory drug-testing regulations. However, research published in 2007 by Bray and Hourani, using the DoD surveys, indicates that the heavy drinking rate among military personnel in 2005 was very similar to the rate in 1980. In a 1992 article Bray and colleagues noted that, although the reduction in alcohol use among military personnel during the 1980s was similar to the decrease among civilians, controlled analyses revealed that those in the military were still more likely to be heavy drinkers than civilians. Additionally, heavy alcohol use among military personnel increased between 1998 and 2005, according to Bray and Hourani's 2007 study using the 2005 DoD survey and the 2004 NSDUH. In 2006 Bray and his colleagues reported a standardized comparison of military personnel and civilians that again revealed a higher percentage of heavy drinkers in the military. When the samples were stratified by age group, the difference was only significant for personnel aged 18 to 25.

Tobacco trends reflect a decline since 1980 as demonstrated by Bray and Hourani in 2007, but are more similar to those of alcohol with respect to civilian comparisons. In the standardized comparison of military and civilian substance use in 1985 by Bray and others in 1991, military personnel were more likely to report any smoking or heavy smoking than civilians. Further, Bray and Hourani's 2007 analysis of the most recent DoD survey indicates that for the first time since 1980, between 1998 and 2002 there was an increase in smoking rates among military personnel from 29.9 percent to 33.8 percent. In 2005 cigarettes were used more often than alcohol, with 32.2 percent of service personnel reporting use in the previous 30 days. A standardized comparison between military and civilian populations by Bray and others in 2006 showed that although service members aged 26 to 55 reflect a similar rate of smoking, the rate for service members aged 18 to 25 was higher than that of civilians.

In 2000 Bray and Marsden stated that the demographic composition of the military had changed; potential reasons they described include the abolition of the draft and the resulting career-oriented workforce. Using DoD data collected between 1980 and 1995 standardized to the first year by demographic composition, they found that although cigarette use and illicit drug use have demonstrated declines, heavy drinking has remained more consistent. Bray and colleagues (2000) hypothesize that a possible reason for the reduction in the use of illicit drugs may be effective military policies. In contrast, the authors state that the declining trend for heavy alcohol use may be accounted for in part by demographic changes in the military.

Bray and colleagues (1991) have also argued that while the military policy of drug testing may have been a significant deterrent to drug use, other aspects of military life may be influential in higher smoking and drinking rates compared to civilians. In 2007 using DoD survey data, Bray and Hourani indicated that it was likely that at least one in six military personnel in 2005 was a heavy drinker. Explanations for the increase in cigarette and heavy alcohol use offered by Bray and colleagues (2007) included demanding recruitment goals, possibly reaching a population that already had these habits. The authors suggested that specific increases between 1998 and 2002 may have been due to increased stress related to preparations for Afghanistan operations in 2001 while the similarity or decrease of rates of these substances between 2002 and 2005 may be the result of reduced access during operations. In a previous study published in 1999, military personnel of both genders were more likely to report that their military duties were stressful compared to their personal lives, and Bray, John A. Fairbank, and Marsden further found that stress related to work or the military was associated with increased likelihood of substance use.

THE IMPACT OF DEPLOYMENT

The impact of deployment on substance use has also been examined. Using the Millennium Cohort study, a sample of active duty personnel and members of the reserves or guard that oversampled for those deployed between 1998 and 2000 to southwest Asia, Bosnia, or Kosovo, Riddle and others (2007) discovered that alcohol abuse was by far the most reported disorder in the study, which used the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PHQ). The prevalence for alcohol abuse was 12.6 percent with the

next largest percentage being 3.2 for major depressive disorder. However, personnel recently deployed to southwest Asia, Bosnia, or Kosovo did not report higher rates of alcohol abuse than those who had been deployed earlier. In contrast, E. Belle Federman, Bray, and Larry A. Kroutil's 2000 article that described a study of active duty personnel, employing the DoD survey from 1995, showed that deployment in the last 30 days was associated with higher rates of heavy alcohol use among men and women. Bray and colleagues' 2006 report that used the 2005 DoD survey also listed heavy alcohol use, illicit drug use, and tobacco use among the outcomes reported by higher percentages of personnel deployed within the past three years compared to those who had not deployed. Specifically, those deployed to Iraq and Afghanistan reported higher rates of heavy alcohol use in the past 30 days and smoking in the past year than those who were not serving in any operations, while those deployed elsewhere reported higher rates of illicit drug use and smoking in the past year compared to those not serving in any operations. However, a slightly lower percentage of personnel reported starting or increasing alcohol use after being deployed than those who reported reducing or stopping alcohol use, with the exception of army personnel.

Potential reasons for the different results may include the composition of the samples: the Millennium Cohort included active duty and reserve/guard personnel whereas the DoD surveys included only active duty service members (Bray et al., 2006; Federman et al., 2000; Riddle et al., 2007). Measurement for each study was different as well. The Millennium Cohort study employed a list of five questions including items addressing whether a series of usual activities had been adversely affected by their drinking. The DoD surveys employed an algorithm based on the frequency and amount of use to create the categories of abstinence, non-heavy use, and heavy use.

Research on deployment and substance use is not limited to alcohol. For example, in a study of naval personnel during the first Persian Gulf War, published in 1996, that included only deployed service members, Lorraine B. Forgas, Mark E. Cohen, and Daniel M. Meyer demonstrated that 7 percent of personnel who smoked began smoking after being stationed in the Gulf. Federman and colleagues (2000) also found an association between deployment and higher rates of smoking among men. In the 1996 Persian Gulf study by Forgas and colleagues, it was found that although 6.2 percent of smoking naval personnel reported quitting or smoking less, slightly less than a third of smoking personnel reported that they smoked more after being stationed there. In contrast, Bray and colleagues (2006) found that a slightly higher percentage of personnel deployed in the previous year reported quitting or smoking less than those who began to smoke or smoke more, with the exception of army personnel.

The most frequent reasons reported by Forgas and colleagues in 1996 for changing smoking habits were stress and boredom. Bray and colleagues (2006) reported that in the 2005 DoD survey, deployment was the second most often reported stressor, behind that of being away from family. This finding is similar to that of Federman and colleagues in 2000 regarding reasons for an association between substance use and deployment. They concluded that stress and length of deployment provided a portion of the explanation for the association between deployment and increased substance use, but asserted that there were other important unmeasured factors that may have accounted for this. In their discussion, the authors suggest examining potential changes in norms and attitudes toward substance use during deployment.

DRUG AND ALCOHOL ABUSE AMONG MILITARY VETERANS

One of the most intensely studied groups of military personnel has been Vietnam veterans. Although narcotic use was widespread among service members during this conflict, Lee N. Robins, John E. Helzer, and Darlene H. Davis's 1975 study of military personnel returning from Vietnam in September 1971 reports that alcohol use and marijuana use were even more common. Christian Ritter, Richard R. Clayton, and Harwin L. Voss (1985) indicated that marijuana use during the Vietnam War may have been influenced by time of service. Veterans reporting use of marijuana during their time in the service were more likely to have served in 1970 or later. The authors hypothesized that this related in part to an increase in the availability of marijuana during and after 1970 in Vietnam. Availability has also been cited among the reasons for the

use of narcotics during this conflict. In 1993 Robins asserted that the rate of use was in response to the high availability and low cost of narcotics and possibly the concurrent lack of availability of alcohol for soldiers under the age of 21.

This military engagement also provided insight into the potential protracted effects of substance use and military service. In a study published in 2004 Seth A. Eisen and others estimated a lifetime rate as high as 54.6 percent for alcohol abuse and/or dependence among a large sample of Vietnam War era veterans interviewed in 1992. However, the rate of alcohol abuse and/or dependence at some point during the twelve months preceding the interviews was much lower at 17.3 percent. With respect to narcotics, in 1975 Robins and colleagues indicated that only a small percentage of service members who were addicted in Vietnam were still addicted after they returned to the United States. Considering veterans more broadly, Todd H. Wagner, Katherine M. Harris, Belle Federman, Lanting Dai, Yesenia Luna, and Keith Humphreys (2007) used the National Household Survey of Drug Abuse (NHSDA) data from 2000 to 2003 and estimated higher rates of heavy drinking for veterans (7.5%) compared to nonveterans (6.5%). A study done by Jillian C. Shipherd, Jane Stafford, and Lynlee R. Tanner in 2005 that was restricted to Persian Gulf War veterans indicated higher rates of substance use problems during the six years following return from service in 1991, with 14–15 percent and 2–3 percent of the sample subscribing to alcohol and drug problems, respectively.

MENTAL HEALTH DIAGNOSES AND ALCOHOL AND DRUG USE

As noted by Denise B. Kandel, Fung-Yea Huang, and Mark Davies in 2001, substance dependence demonstrated associations with increased odds of a probable psychiatric disorder, such as depressive or anxiety syndromes using data from the 1994 to 1996 NHSDA. Substance abuse and affective disorders were among the conditions identified as having high non-combat related impact on the health of U.S. military members in John F. Brundage, Karen E. Johnson, Jeffrey L. Lange, and Mark V. Rubertone's 2006 analysis of 2002 data from the Defense Medical Surveillance System. Alcohol disorders were, by far, the most common mental disorders reported as a primary diagnosis among all active-duty personnel from 1990 to 1999 in both hospitalizations and number of ambulatory visits, according to Charles W. Hoge and colleagues in 2002. Alcohol and substance abuse also have implications for other psychiatric outcomes. Using data from the Veterans Affairs National Registry for Depression collected between 1999 and 2004, Kara Zivin and colleagues reported in 2007 that any diagnosis of alcohol or substance abuse in the 12 months preceding study entry through the study period was associated with a higher rate of suicide among depressed patients. Paige C. Ouimette, Pamela J. Brown, and Lisa M. Najavits's review of the literature published in 1998 about the course and treatment of patients with substance use and post-traumatic stress disorder (PTSD) across multiple samples, including veterans in Veterans Affairs treatment centers, noted that substance abuse patients with PTSD may be more vulnerable to poorer post-treatment outcomes.

DEMOGRAPHIC PATTERNS IN DRUG AND ALCOHOL ABUSE

Over the period from 1980 to 1992, men in the military demonstrated a greater rate of heavy alcohol use than women, although rates of illicit drug use across gender were similar during much of that period according to Bray, Kroutil, and Marsden (1995). An analysis of data by Bray and colleagues from the DoD survey in 1995 published in 1999 demonstrated that while men and women were similar in rates of illicit drug use, men were slightly more likely to smoke and were more than three times as likely to be heavy drinkers. Bray and others reported (2006) that in 2005 the greatest distinction in rate of heavy drinking between civilians and military personnel appeared to be among males between the ages of 18 and 25 serving in the U.S. Army and Marine Corps in stratified analyses. The percentage of female military personnel and female civilians aged 18 to 25 who engaged in heavy drinking were similar except among women in the Marine Corps, who exhibited a higher rate than civilian women.

Although military duties were associated with stress in both genders, the reasons reported for stress that were associated with substance use varied by gender according to Bray and others in 1999. For example, one-third of the women reported they experienced high stress specifically

related to being a woman in the military; experiencing high levels of this type of stress was associated with increased odds of illicit drug use in the past 12 months and cigarette use in the past month compared to experiencing low levels. Military men experiencing high stress at work were more likely to report heavy alcohol or cigarette use in the past month and illicit drug use in the past 12 months compared to men experiencing low stress at work.

OTHER ADDICTIONS NOT READILY DIAGNOSABLE

Some addictions that are not readily apparent have been examined among military personnel. Benjamin W. Lacy and Thomas F. Ditzler argued in 2007 that the use of inhalants can affect military readiness and impact service members' health but that inhalants have received less attention than other drugs as far as prevention, detection, and treatment. The authors hypothesized that the short-lasting effects and the ability to return to work without appearing intoxicated may be attractive to military personnel. In 2006 Bray and others reported the prevalence of active military service members reporting inhalant use in the past 12 months during 2005 was highest among Marines (3.4%) while the overall prevalence was 2.1 percent. Gambling has also been studied among military personnel. The prevalence of active military service members answering affirmatively to one of ten questions assessing gambling-related problems in 2002 was 6.3 percent, according to Bray et al. (2003). Only 1.2 percent answered affirmatively to five or more questions, an indication of probable pathological gambling. The 2003 published report of the 2002 data also described how in previous years, prevalence of three affirmative responses was reported, and this rate remained consistent at approximately 2 percent across 1992, 1998, and 2002.

TREATMENT AND PREVENTION STRATEGIES

In a discussion of the progress that has been made among military personnel in the U.S., in 1992 Bray and colleagues summarized DoD directives and sinstructions in the four major program areas that the military highlights: assessment, deterrence and detection, treatment and rehabilitation, and education and training. Methods of carrying out these directives include the Worldwide Surveys, background checks, initial and random drug tests, the operation of a large drug and alcohol abuse treatment and rehabilitation program, and the provision of education and training. There is also treatment available for non-substance addictions. For example, in a 2004 article, Otto Kausch reported that one veterans' hospital has offered treatment for gambling since 1972. Treatment specifically for gambling offered overseas within the Substance Abuse Rehabilitation Program inside the navy has been described by Carrie H. Kennedy, Jeffrey H. Cook, Daniel R. Poole, Christopher L. Brunson and David E. Jones in 2005. However, it was also reported that service members seeking help for gambling express fear of discovery. Similarly, it has also been found that potential disciplinary action or concern for their military career may prevent personnel from seeking treatment for substance use (Bray et al., 1992).

In 1993 Robins argued that availability is the main explanation for the increased prevalence of narcotic use and addiction among the military population during the Vietnam War. This idea has also been discussed in reference to alcohol. In 1992 Bray and colleagues stated that a number of people in the military believe that policies such as setting hours and prices for alcohol sales and policing the availability of drugs have affected the accessibility of these substances. However, there may be room for further improvement. For example, in 1996 Forgas and colleagues conducted a study of naval personnel during the Persian Gulf War. They found that, although nearly a quarter of the sample stated that military efforts to influence them to quit their tobacco habits were successful, sailors paid much less for cigarettes than civilians and some also reported receiving free cigarettes from the United Service Organizations (USO) and tobacco companies.

CONCLUSION

The military has made great strides toward reducing the rate of illicit drug use. These same reductions have not been achieved in heavy drinking and tobacco use. In this, the armed forces face the same challenge as civilians: discouraging the use and abuse of licit drugs. In contrast, military personnel must resist using drugs and alcohol to cope with the unique challenges related to military life. In 2005 Bray and others (2006) reported that more than 25

percent of military personnel used alcohol or tobacco as coping mechanisms. It is clear that the United States military must expand its efforts to improve the reduction of substance use and abuse.

See also **Addiction: Concepts and Definitions; Alcohol: Psychological Consequences of Chronic Abuse; Cocaine; Coping and Drug Use; Depression; Drug Testing Methods and Clinical Interpretations of Test Results; Gambling; Marijuana (Cannabis); Risk Factors for Substance Use, Abuse, and Dependence: Stress; Suicide and Substance Abuse; Tobacco: Dependence; U.S. Government Agencies: Substance Abuse and Mental Health Services Administration (SAMHSA); Vietnam Era Study (VES), Washington University; Vietnam War: Drug Use in U.S. Military; Women and Substance Abuse.**

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LARA M. DEPADILLA

MINI INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW (MINI).

Structured diagnostic interviews were first used to standardize the collection of diagnostic information in psychiatric epidemiology studies. They are used frequently in multicenter, research treatment studies to standardize diagnostic eligibility criteria across sites, often in different countries and languages. They are used to improve diagnostic precision and to track a patient's progress in non-research settings. Examples include the diagnostic assessment of individuals applying for disability benefits, of people in correctional/prison systems, of military personnel entering and exiting theaters of conflict, in mental health screening institutions, and by managed health-care organizations and health-care delivery systems. Unlike the usual clinical interview, structured diagnostic interviews allow comparison across clinical centers, reduce variability in diagnosis, and help to improve quality of care.

HISTORY AND EARLY LIMITATIONS OF STRUCTURED INTERVIEWS

The early structured interviews had many limitations. They were often long, cumbersome, and required considerable training and expertise. These interviews included the Present State Exam (PSE), Diagnostic Interview Schedule (DIS), the Schedule for Affective Disorders and Schizophrenia (SADS), the Composite International Diagnostic Interview (CIDI) or Schedule for Clinical Assessment in

Neuropsychiatry (SCAN), and the Structured Clinical Interview for *DSM-III-R* (SCID). These interviews often took forty-five minutes or longer to administer.

Shorter structured diagnostic interviews, taking five to fifteen minutes to administer, were designed for primary care settings. These included the Symptom Driven Diagnostic System (SDDS) and the Primary Care Evaluation of Mental Disorders (Prime MD), which collected information on six major Axis I disorders.

In the early 1990s, with the globalization of health-care research, researchers from academia, regulatory agencies, national institutes, and the pharmaceutical industry thought there was a need for a structured interview that would bridge the gap between the older, detailed, time-consuming, diagnostic interview and the ultra short screening tests designed for primary care.

Disorder	Time Frame
1 Major Depressive Episode	Current (2 weeks), Recurrent and Past
2 Suicidality	Current (Past Month)
3 Manic Episode	Current and Past
Hypomanic Episode	Current and Past
4 Panic Disorder	Current (Past Month)
5 Agoraphobia	Current
6 Social Phobia (Social Anxiety Disorder)	Current (Past Month)
7 Obsessive-Compulsive Disorder	Current (Past Month)
8 Posttraumatic Stress Disorder	Current (Past Month)
9 Alcohol Dependence	Past 12 Months
Alcohol Abuse	Past 12 Months
10 Drug Dependence	Past 12 Months
Drug Abuse	Past 12 Months
11 Psychotic Disorders	Lifetime and Current
Mood Disorder with Psychotic Features	Current
12 Anorexia Nervosa	Current (Past 3 Months)
13 Bulimia Nervosa	Current (Past 3 Months)
14 Anorexia Nervosa, Binge Eating/ Purging Type	Current
15 Generalized Anxiety Disorder	Current (Past 6 Months)
16 Antisocial Personality Disorder	Lifetime

Table 1. Disorder diagnoses available on the MINI 6.0.0
ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

MINI DEFINED AND DESCRIBED

The Mini International Neuropsychiatric Interview (MINI) is a structured psychiatric interview for adults, which takes approximately fifteen minutes to administer. It assesses fifteen major Axis I disorders and one Axis II disorder (see Table 1). Validation and reliability studies have been done comparing the MINI to the SCID-P for *DSM-III-R* and the CIDI. The results of the studies showed that the MINI has acceptable high validation and reliability scores but can be administered in a much shorter period of time than the above referenced instruments. The MINI is short, inexpensive, simple to use, clear, easy to administer and to navigate, highly sensitive (a high proportion of patients with a disorder are detected) and specific (it has the ability to screen out patients without disorders). The MINI is compatible with international diagnostic criteria, including the *International Classification of Diseases* (*ICD-10*) as well as the *Diagnostic and Statistical Manual of Mental Disorders,* fourth edition, (*DSM-IV*). It is also able to capture important subsyndromal variants and is useful in both clinical psychiatry and in research settings.

The MINI is divided into modules identified by letters, each corresponding to a diagnostic category. At the beginning of each diagnostic module (except for the psychotic disorders module), screening questions corresponding to the main criteria of the disorder are presented in a gray box. At the end of each module, diagnostic boxes permit the clinician to indicate whether diagnostic criteria are met.

The MINI was not intended to replace the psychiatrist or physician. Rather, like a laboratory test in medicine, it is designed to capture routine and repetitive information, maximizing the efficiency of the medical encounter and leaving specialists time for other critical tasks. The MINI was designed to be administered by psychiatrists, psychologists, physicians, or by trained nurses or health information technicians. The MINI is not suitable for administration by lay interviewers because it requires clinical skill and experience to implement properly. Another limitation of the MINI is that it only covers 16 of the most common Axis I disorders. Many Axis I disorders are not screened by the MINI.

While the MINI questions patients about the presence or absence of *DSM-IV* criteria for alcohol and drug abuse and dependence, it is entirely dependent on the veracity of the patient for accuracy. It should never be construed as an adequate substitute for laboratory screening (urine and blood levels) of alcohol and drugs (which, of course, have their limitations as well).

The developers of the MINI included many suggestions and improvements offered by colleagues around the world, which led to the MINI "Family" of rating scales and to ever more useful versions.

The MINI Plus has 26 modules and covers 62 disorders and subtypes. It assesses all the subtypes and timeframes as well as all the disorders that might be reasonably included in clinical research studies. Even though the MINI Plus covers many more disorders, the format is less complex and easier to navigate than that of the other longer interviews.

The MINI Screen is a short, one page (two sides) screening instrument that is designed to assess patients quickly and determine if there might be further need for structured evaluation. It uses only the screening questions from the full MINI.

The child/adolescent variant of the MINI, called the MINI-KID is a structured diagnostic instrument for psychiatric disorders in children and adolescents. The questions are based primarily on those of the MINI but are phrased in a language easy for children to understand. The MINI-KID includes eight additional modules for disorders frequently found in children and adolescents such as attention deficit hyperactivity disorder, tic disorders, and conduct disorder. The MINI-KID is shorter and easier to administer than the other structured interviews available as of 2008 for children and adolescents. A validation and reliability study completed in 2007 compared the MINI-KID with the Kiddie-SADS. The MINI-KID had acceptable validity and reliability scores and could be administered in one-third the time of the Kiddie-SADS.

AVAILABILITY

As of 2008, the MINI was available in over fifty different languages. It was also available in a computerized form (eMINI) that could be integrated with medical screening or triage of large samples of patients. The computerized version is faster to implement in practice than the paper version because all the calculations and algorithms are calculated automatically in the background for the user, it prints out a clean copy of the executed interview, and stores all data for future export and analysis. The MINI is designed to be used in a variety of situations, from clinical research to actual clinical practice when a diagnosis is in question, from tracking patients over time to computerized monitoring of patients in quality improvement programs. The Web site maintained by Medical Outcomes Systems provides more information about the MINI and allows free downloading of the different MINIs.

As of 2008, professionals anticipated increasing use of structured diagnostic interviews in electronic form for large-scale population screening and early detection of suicide risk and mental health.

See also **Diagnostic and Statistical Manual (DSM); International Classification of Diseases (ICD).**

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MINIMUM DRINKING AGE LAWS.

Before the twentieth century, there were few legal restrictions on the consumption of alcoholic beverages by youth. Early in the twentieth century, laws prohibiting alcohol sales to minors began to be implemented as part of a broader trend of increasing legal controls on adolescent behavior. The temperance movement worked to establish national prohibition in 1919 but when the Eighteenth Amendment was repealed in 1933, all states implemented legal minimum ages for alcohol purchase or consumption, with most states setting the age at twenty-one.

From the 1930s through the 1960s, the issue received little public attention. In 1970, the Twenty-Sixth Amendment to the U.S. Constitution lowered the voting age in federal elections from twenty-one to eighteen. By 1974, all fifty states had lowered their voting ages for state elections to eighteen. As part of this trend of lowering the age of majority, twenty-nine states lowered their minimum drinking ages between 1970 and 1975, most setting the age at eighteen or nineteen. In the mid-1970s, studies began to emerge that showed significant increases in the rate of young drivers' involvement in traffic crashes following the reductions in the legal drinking age. The trend toward lower drinking ages was reversed, with Maine being the first state to raise its legal drinking age from eighteen to twenty in October 1977. Several other states soon followed, and research studies completed by the early 1980s found significant declines in youth traffic-crash involvement after states raised their legal drinking age. With the support of organized efforts by such citizen-action groups as Remove Intoxicated Drivers and Mothers Against Drunk Driving, federal legislation was passed in 1984 that called for the withholding of a portion of federal highway-construction funds from any state that did not have a legal drinking age of twenty-one by October 1986. As a result, all the remaining states with a lower legal drinking age raised their minimum age to twenty-one by 1988. Thus, all states as of 2008 have a uniform legal drinking age of twenty-one, although details in regard to the purchase, possession, consumption, sales, and furnishing of alcohol to underage youth vary from state to state.

The legal drinking age became a major issue because of the serious consequences of young people's consumption of alcohol. Most teenagers drink; in addition, almost one-third become regularly intoxicated (Johnston et al., 2007). Such use is not without considerable expense. Car crashes are the leading cause of death for teenagers, and nearly one-fourth of youth in fatal traffic crashes have been drinking (National Highway Traffic Safety Administration, 2006).These intoxicated drivers are a danger to themselves and a considerable danger to others, as half the people who die in crashes involving an underage drinking driver are people other than the driver (U.S. Department of Transportation, 2004). Other leading causes of death and disability among youth, such as suicide, homicide, assault, drowning, and recreational injury involve alcohol in one-fourth to three-fourths of cases (Smith et al., 1999). Injuries are only part of the problem. Early use of alcohol appears to affect multiple dimensions of physical, social, and cognitive development. Alcohol increases the odds of having unprotected sex (i.e., failure to use a condom); multiple partners; pregnancy; and contracting sexually transmitted diseases, including the human immunodeficiency virus (HIV; Cook & Clark, 2005; Dunn et al., 2003; Guo et al., 2002; Stueve & O'Donnell, 2005). Further, nearly three-fourths of date-rape situations involve individuals who have been drinking (Mohler-Kuo et al., 2004). Early use of alcohol increases the odds one will move on to using other drugs, such as marijuana, cocaine, or heroin (Kandel, 2002) and increases the

likelihood of later addiction and criminal and violent behavior (Brown et al., 2000; Ellickson et al., 2003; Monti et al., 2005; Warner & White, 2003).

Additionally, research has shown that exposure to alcohol in adolescence can have detrimental long-term effects on brain development and intellectual capabilities (Brown et al., 2000; Monti et al., 2005). Despite the many problems associated with young people's drinking, the most obvious one, and the one that received the most attention in debates on the legal drinking age, is traffic-crash involvement.

EFFECTS OF THE DRINKING AGE ON CAR CRASHES

The legal drinking age is one of the most extensively researched policies designed to reduce traffic crashes and other alcohol problems, with nearly 150 empirical evaluations published since the early 1970s. Sixty-one published studies have assessed effects of changes in the legal minimum drinking age on indicators of driving after drinking and traffic crashes, providing over one hundred estimates of effect. While results vary across studies and across states, the preponderance of evidence indicates an inverse relationship between the minimum legal drinking age and traffic crashes: When the legal age increased, crashes decreased.

Twelve studies have examined the effects of lowering the minimum drinking age (usually from age twenty-one to eighteen) and most (exceptions are Bellows, 1980; Naor & Nashold, 1975) reported increases in fatal and injury-producing traffic crashes likely to involve alcohol (e.g., single-vehicle crashes occurring at night) following a decrease in the legal drinking age. Across all outcomes studied, over half (52 percent) of observed effects were statistically significant, with increases in youth involvement in fatal traffic crashes ranging from 2 to 30 percent (Shults et al., 2001).

Forty studies of the effects on traffic crashes of raising the legal age for drinking were published between 1979 and 2007. Nearly all found reductions in the involvement of youth in traffic crashes following increases in the legal drinking age (exceptions are Chung, 1997; Davis & Reynolds, 1990; Hughes & Dodder, 1992; Jones et al., 1992; Vingilis & Smart, 1981). Across all outcomes studied, 57 percent of observed effects were statistically significant. Typically, raising the drinking age resulted in a 6 to 30 percent reduction in traffic crashes likely to involve alcohol (Shults et al., 2001).

Scientists and professionals in the field agree that lowering the legal age for drinking increased car crashes among youth and that subsequently raising the legal age reversed the effect: It lowered car crashes among youth (National Research Council and Institute of Medicine, 2004). There is a large, fairly consistent body of scientific literature substantiating these relationships, with 98 percent of all analyses reporting statistically significant effects finding higher drinking ages associated with lower rates of traffic crashes (Wagenaar & Toomey, 2002). The National Highway Traffic Safety Administration estimates that the U.S. age-twenty-one policy has saved nearly 22,000 lives, averaging over one thousand lives per year, in reduced car crashes alone (Kindelberger, 2005).

EFFECTS OF THE DRINKING AGE ON OTHER PROBLEMS

Thirty-one studies have examined effects of changes in the legal drinking age on indicators of other health and social problems. Among these thirty-one studies, there are over sixty estimates of effects on social and health outcome measures, including violence, homicide, suicide, and unintentional injury, and results are less consistent than those for traffic crash outcomes. Of all analyses that reported statistically significant effects, approximately 75 percent found higher drinking ages associated with lower rates of problems. Over 70 percent of analyses found no statistically significant association between the legal drinking age and indicators of other health and social problems; some of the studies had low power to detect effects.

EFFECTS OF THE DRINKING AGE ON ALCOHOL USE

Twelve studies examined the effect of the legal drinking age on aggregate alcoholic-beverage sales. Effects were mixed: Some studies found that alcohol sales were significantly inversely related to the legal age whereas others did not find such a relationship. These studies are difficult to interpret, as alcohol sales to young drinkers could not be distinguished from sales to older drinkers.

The effects of the legal minimum drinking age on self-report measures of alcohol consumption

among youth are more prolific and have produced conflicting results. Forty-two studies assessing effects of changes in the legal minimum drinking age on self-reported indicators of alcohol consumption were published between 1975 and 2007, providing over sixty empirical estimates of effect. Among these studies, half found an inverse relationship between the legal drinking age and alcohol consumption; that is, as the legal age was lowered, drinking increased, and as the legal age was raised, drinking decreased. A major limitation of many of these studies was their use of nonrandom samples of youth from particular high schools, colleges, and local communities rather than samples that were broadly representative of the youth in a state (Wagenaar & Toomey, 2002). Surveys of college students, which are usually limited to students in introductory social science courses, frequently report finding little effect of the legal drinking age on drinking patterns. In contrast, surveys of random samples of high school seniors and eighteen- to twenty-year-olds across many states, including those entering college and those in the workforce, report finding significant reductions in drinking that are associated with higher legal drinking ages (Maisto & Rachal, 1980; O'Malley & Wagenaar, 1991; Wagenaar & Toomey, 2002). It appears on the basis of the best-designed studies that raising the legal drinking age resulted in important reductions in young people's drinking. The age-twenty-one policy, however, by no means eliminates drinking by youth.

ENFORCEMENT OF THE MINIMUM DRINKING AGE

While there were slight declines in the 1990s and early 2000s, alcohol remains the drug of choice among youth in the United States. When questioned, 45 percent of high school seniors reported drinking in the last month, and 30 percent reported having had five or more drinks at a time at least once in the previous two weeks (Figures 1 and 2; data from Johnston et al., 2007). Among the many reasons for youth alcohol consumption, one important reason is that alcohol remains easily accessible. Published studies indicate that despite the minimum legal age of twenty-one, underage buyers are able to purchase alcohol in many communities without showing age identification in 47 to 97 percent of attempts (Forster et al., 1994; Grube, 1997; Paschall et al., 2007; Preusser & Williams, 1992).

It is notable that effects discussed here have been achieved with only modest (at best) enforcement of this law. While studies of enforcement effects are few, results show that enforcement has reduced illegal sales to youth (Grube, 1997; Huckle et al., 2005; Lewis et al., 1996; Scribner & Cohen, 2001; Wagenaar et al., 2005; Wilner et al., 2000). One study by Wagenaar and associates (2005) indicated that enforcement of the legal drinking age produced an immediate 17 percent reduction in the likelihood of sales to minors, with effects decaying within three months. Thus, enforcement needs to be ongoing to prevent the illegal sales of alcohol to teens.

Strong evidence showing that raising the drinking age to twenty-one reduced deaths and injuries in car crashes was a major factor in the debate about the drinking age. Other arguments were also heard, such as those that asked if it is unconstitutional to discriminate solely on the basis of age. Federal courts have ruled that the drinking age is not discriminatory because: (1) drinking is not a fundamental right; (2) age is not an inherently suspect criterion for discrimination; and (3) the higher drinking age has a rational basis and is reasonably related to a legitimate goal of the state to reduce death and injury from traffic crashes (Wagenaar & Toomey, 2002). In a democracy, laws should have the support of the governed. Repeated polls from the 1980s to early 2000s have shown that the majority of those asked clearly support a legal drinking age of twenty-one. Even among youth under the age of twenty-one, polls have shown majority support for this minimum drinking age.

Some people wonder if it is logical to set the legal age of drinking at twenty-one when other rights and privileges of adulthood (e.g., voting, signing legally binding contracts, enlisting in the armed forces) begin at age eighteen. Others answer that it is because there are many different legal ages, varying from twelve to twenty-one, for voting, driving, sale and use of tobacco, legal consent to sexual intercourse, marriage, access to contraception without parental consent, compulsory school attendance, and so forth. Minimum ages are not set uniformly; they depend on the specific

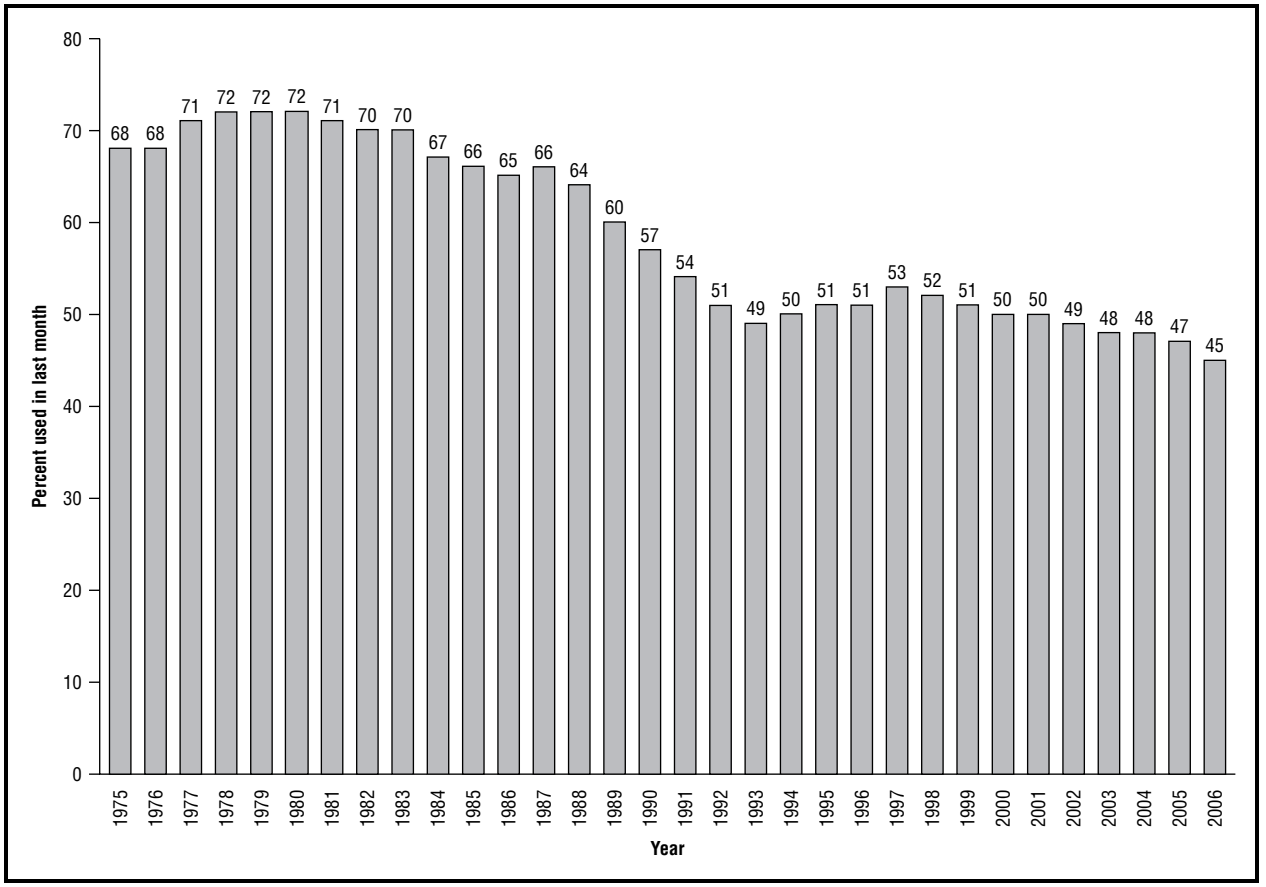

Figure 1. Percent of high school seniors reported drinking in the last month. (Source: Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2007). *Monitoring the future: National results on adolescent drug use: Overview of key findings, 2006.* Bethesda, MD: National Institute on Drug Abuse. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

behavior involved, and they are determined by balancing the dangers and benefits of establishing the particular age.

Some have argued that a minimum drinking age of twenty-one will make matters worse when young people finally get legal access to alcohol. The idea here is that prohibiting teenagers from drinking causes a pent-up demand for alcohol as a forbidden fruit. At twenty-one, young adults will break loose and drink at significantly higher rates than they would have if they had been introduced to alcohol earlier. This theory is clearly not supported by research. For example, O'Malley and Wagenaar (1991) found just the opposite results in their nationwide study; that is, persons aged twenty-one to twenty-four drank at *lower* rates if they had to wait until twenty-one to have legal access to alcohol. A frequently heard related argument is that a minimum drinking age of twenty-one may reduce car crashes among teenagers, but this will only be a temporary effect if it simply delays those problems until the teenagers reach age twenty-one. This argument also proves false. The minimum age of twenty-one significantly reduces car crashes among eighteen- to twenty-year-olds, and those injuries and deaths are permanently saved. There is furthermore no rebound effect at age twenty-one; in fact, the higher legal age appears to produce benefits that continue into a person's early twenties.

While the debate around the legal age for drinking appeared to be settled in the United States as of 2008, there are a few observers who are again voicing support for lowering the drinking age, arguing the U.S. has a continuing problem of teen drinking, and they posit that a lower drinking age might help. However, such a hypothesis ignores much of the scientific literature and the

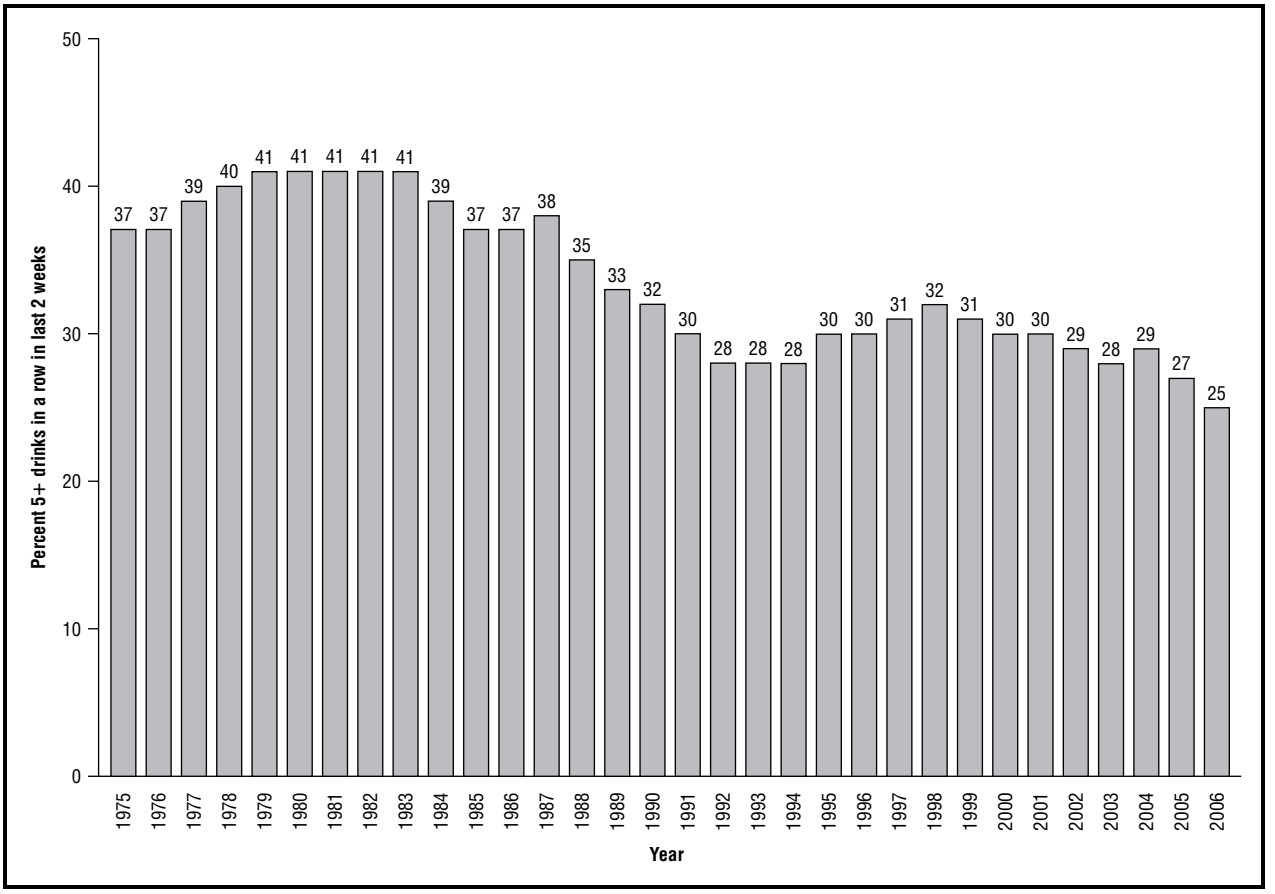

Figure 2. Percent of high school seniors reported having had five or more drinks at a time at least once in the previous two weeks. (Source: Johnston, L. D., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. E. (2007). *Monitoring the future: National results on adolescent drug use: Overview of key findings, 2006.* Bethesda, MD: National Institute on Drug Abuse. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

direct experience obtained when states last experimented with the legal age in the 1970s and 1980s.

Professionals in the areas of public health and traffic safety, as well citizens, have realized the benefits of the age-twenty-one drinking law in the United States. Other countries are examining the experience in the United States, and are actively considering raising their legal age. The preponderance of evidence indicates that there is an inverse relationship between the minimum legal drinking age and two important outcomes: alcohol consumption and traffic crashes. Compared with a wide range of other programs and efforts to reduce drinking among teenagers, research shows increasing the legal age for purchase and consumption of alcohol to twenty-one has been the most successful prevention effort in decades. Considering the benefits that have been achieved with only modest enforcement, there is great opportunity to even further reduce underage alcohol consumption, traffic crashes, and lives lost.

See also **Accidents and Injuries from Alcohol; Driving, Alcohol, and Drugs; Driving Under the Influence (DUI); Legal Regulation of Drugs and Alcohol; Prohibition of Alcohol; Social Costs of Alcohol and Drug Abuse; Temperance Movement.**

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MINNESOTA MULTIPHASIC PERSONALITY INVENTORY. The MMPI was developed by Starke R. Hathaway and J. Charnley McKinley and first published in 1942 for the diagnosis of a variety of mental disorders and psychopathology. In its current form, the MMPI-2 (1989) is a self-report test containing 567 true/false items administered in 60–90 minutes and in a variety of formats: pen and pencil, computer, or audiocassettes (Butcher et al., 1989). As one of the most widely used personality assessment tools, the MMPI-2 is sometimes administered to individuals who abuse alcohol or drugs and to identify personality characteristics associated with the abuse.

The MMPI-2 has ten clinical scales that generate a profile identifying the patient's personality traits and disorders in relation to population norms. These norms were derived from normative samples consisting of adults aged 18–80 from diverse communities and regions across the United States. The clinical scales are: Hypochondriasis, Depression, Hysteria, Psychopathic Deviate, Masculinity-Femininity, Paranoia, Psychasthenia (a neurotic disorder with chief characteristics that include the presence of phobias, obsessions, and great anxiety), Schizophrenia, Hypomania, and Social Introversion. In addition, the MMPI-2 has several other scales, clinical subscales and newly developed supplementary scales, such as the Addiction Admissions Scale (AAS) and the Addiction Potential Scale (APS) to help validate and expand clinical diagnoses and enhance interpretation of the main clinical profile (Weed et al., 1992).

The MMPI-2 has three main applications to the evaluation, diagnosis, and study of substance-use disorders. First, it has been used to evaluate the effects of alcohol and drug abuse. Several studies (e.g., Babor et al., 1988) have shown that MMPI clinical scales measuring depression, paranoia, and other psychiatric symptoms tend to be higher than normal when alcoholics are drinking—but return to the normal range during periods of abstinence. Second, research on the MMPI has used cluster analysis to identify subtypes of alcoholics and drug users (e.g., Belding et al., 1998, Moss & Werner, 1992). For example, three types of alcoholics were identified based on their MMPI profiles: neurotic, psychotic, and psychopathic (Robyak et al., 1984). Third, the MMPI-2 has been used in the development of special scales for drug and alcohol abuse. The MacAndrew Alcoholism Scale (MAC) is used to measure impulsivity, pressure for action, and acting-out potential that may lead to alcoholism (Craig, 2005; MacAndrew, 1965). Similar to the MAC, the APS was designed to identify personality traits and factors that play a role in the addictions. The APS assesses the individual's acknowledgement or denial of substance abuse. The MMPI-2 can be used in research, but it is mostly used in clinical settings for intake assessments. The clinical profile generated by the MMPI-2 helps to determine and guide treatment plans.

See also **Addiction Severity Index (ASI); Diagnostic and Statistical Manual (DSM); Michigan Alcoholism Screening Test (MAST); Models of Alcoholism and Drug Abuse.**

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MODELS OF ALCOHOLISM AND DRUG ABUSE.

The development of conceptual models that define the essential characteristics of alcoholism and addiction has been an enduring preoccupation of drug and alcohol studies. The question of whether substance dependence is best conceptualized as a disease, a syndrome, a learned behavior, a bad habit, or a social process continues to produce discussion and dissent. Indeed, the debate concerns not only the nature of alcoholism addiction, but also the implications of different models. Does a disease model of addiction necessarily support medical treatment as the most effective intervention? Does it endorse abstinence as the only viable treatment goal? Does it undermine or enhance the stigma of addiction? Is a syndrome a disease by another name, or does it represent a challenge to the notion of a singular disease? Consensus is unlikely because of the different functions served by various models and the range of groups that have a stake in the issue. However, the articulation and refinement of conceptual frameworks is valuable in itself, and is characteristic of a vibrant research field. The adoption of different frameworks also has an impact on treatment and policy decisions, thereby affecting the experiences of those with drug and alcohol problems.

Rather than providing a comprehensive account of all current models of alcoholism and drug dependence in the following entry, it is important instead to focus on key approaches. It is possible to identify recurring (and recurringly contested) themes in definitions of alcohol and drug dependence: loss of control, craving, continued use despite harmful consequences, evidence of biological alteration such as withdrawal symptoms or tolerance, and individual vulnerability to dependence. The conceptualization of alcoholism as a disease is a central focus because it has been so prominent as "a governing image" of scientific and lay attempts to prevent and understand problem drinking and drug consumption (Room, 2001).

FROM SIN TO SICKNESS

Histories of addiction generally begin with the shift from pre-modern views of excessive drinking and drunkenness as willful and immoral conduct to the notion of alcoholism as a "disease of the will," (Valverde, 1998). According to Harry G. Levine's influential article (1978), "The Discovery of Addiction," the idea that habitual drunkenness represented a loss of control over drinking, occurred at the end of the eighteenth century, with the rise of the middle classes and the ideology of bourgeois individualism. Prior to this time people thought drunkards drank to excess because they chose to indulge in a pleasurable sin.

A key figure in the promotion of the new view of inebriety was the prominent American physician Benjamin Rush. Rush—who published his "Inquiry into the Effects of Ardent Spirits" in 1784—unified several ideas into a new paradigm to provide "the first clearly developed modern conception of alcohol addiction" (Levine, 1978, p. 151). The main tenets of this paradigm were that (a) chronic drunkenness represented a loss of control over drinking, (b) this condition was a disease with a tendency to progress, (c) "spirituous liquors" were the cause of the disease,

and (d) abstinence was the only cure (Levine, 1978; White, 2000a). These ideas have remained prominent in understandings of addiction, especially the emphasis on compulsion as a feature that distinguishes the state of dependency from other forms of problem drinking.

As the nineteenth century progressed, physicians in both the United States and Britain used increasingly medicalized language to describe patients who exhibited recurring drunkenness. The terms used included "monomania of the will," "dipsomania," "habitual inebriation," and "the disease of inebriety" (White, 2004). The view that drunkenness was a medical problem that should concern doctors was supported by increased awareness of the detrimental physical effects of excessive alcohol intake. In 1849 Swedish physician Magnus Huss published a systematic study of the deleterious effects of alcohol on the body and concluded that these symptoms were "a disease group in themselves" (cited in White, 2000a, p. 49). Huss proposed the name *alcoholism* for this disease. As a disease, inebriety or alcoholism was seen as a treatable condition, and thus the doctors involved in the development of the medical paradigm also campaigned for specialist inebriate asylums (Valverde, 1998).

While the disease model developed in the nineteenth century is routinely contrasted with moral and religious views of the drunkard, the distinction between the two perspectives is not always clear-cut. The use of medical terminology does not preclude moral judgment, for example, that preachers often used words such as *disease* and *sickness* to describe morally reprehensible behavior without any commitment to a medical perspective (Ferentzy, 2001). Rush labeled chronic drunkenness a "disease induced by an act of vice" (Rush, 1943, p. 337).

In the early twentieth century the view of the addict as a patient deserving sympathy was overshadowed by an emphasis on the addict as a menace to society, reflected in and promoted by the increased criminalization of drug use (Musto, 1999). Disease metaphors were frequently used to demonize addicts and addiction during this period. In the early twenty-first century, the dominance of disease conceptions of addiction in the United States had not prevented the punitive measures and moralized rhetoric of the "war on drugs" (Keane, 2005).

THE MODERN DISEASE CONCEPT

In the mid-twentieth century a new version of the disease concept of alcoholism was developed that emphasized the role of individual vulnerability rather than the pernicious effects of alcohol (Mann et al., 2000). The idea of alcoholism as a disease was promoted and disseminated by scientists and other advocates through institutions such as the Yale Center of Alcohol Studies, the Research Council on Problems of Alcohol, and the National Committee for Education on Alcoholism (White, 2000b). Their advocacy of a scientific approach to the study of alcohol problems appealed to both "wet" and "dry" constituents in the post-Prohibition era (Roizen, 2004; Room, 1983). E. M. Jellinek, head of the Yale Center, was the most influential scientist in the field of alcohol studies, which developed from the alcoholism movement. His *Disease Concept of Alcoholism* (1960) is widely cited as the seminal text in the field, even if much of its detail has been forgotten.

Jellinek (1952) defined alcoholism expansively as any consumption of alcohol that causes damage to the individual or society. He saw it as a condition that progressed in severity through predictable stages of development, analogous to the natural history of a disease. But he classified only two out of five "species" of alcoholism as diseases, because they alone were based on a "physio-pathological process" involving adaptation of cell metabolism; acquisition of tolerance; and experience of withdrawal symptoms, craving and loss of control, or inability to abstain (Jellinek, 1960, p. 40). The World Health Organization (WHO) Committee on Addiction-Producing Drugs also emphasized physiological alteration as the basis of addiction when it set out two diagnostic categories in 1958, drug addiction and drug habituation, the former signifying the presence of both physical and psychological dependence, the latter "only" psychological (Room, 1998).

DEPENDENCE SYNDROME

In response to some of the shortcomings of Jellinek's one-dimensional and broad definition of alcoholism, British psychiatrists Griffith Edwards and Milton Gross proposed an alcohol dependence syndrome in 1976. Rather than a simple categorical definition, the dependence syndrome was a collection of seven elements that could differ in degree, thus allowing

the syndrome to exist in a continuum of severity from mild to severe (Edwards & Gross, 1976, p. 1058). Crucially, the development of dependence resulted from both biological and learning processes. Edwards (1986) later identified the core elements of the syndrome as (a) impaired control over drinking behavior, and (b) withdrawal and its attendant behavior, including the subjective need for alcohol. Another influential aspect of the dependence syndrome model was the differentiation of dependence from heavy drinking and alcohol-related disabilities such as cirrhosis or marital breakdown.

The criteria for alcohol and substance dependence set out in WHO's *International Classification of Diseases* and the American Psychiatric Association's *Diagnostic and Statistical Manual* are largely based on Gross and Edwards's model. The most recent edition of the *International Classification of Diseases* (*ICD-10*) describes substance dependence syndrome as a "cluster of behavioral, cognitive and physiological phenomena that develop after repeated substance use" (World Health Organization, 1992, p. 321). Diagnosis is made if three of the following criteria are met: (a) a strong desire or sense of compulsion to take the substance, (b) impaired capacity to control its use, (c) a physiological withdrawal state, (d) evidence of tolerance, (e) preoccupation with substance use and decreased interest in other activities, and (f) persistent use despite clear evidence of harmful consequences (World Health Organization, 1993, p. 57).

The description in the American Psychiatric Association's most recent diagnostic manual (DSM-IV) is similar, defining substance dependence as "a maladaptive pattern of substance use, leading to clinically significant impairment or distress" (American Psychiatric Association, 1994, p. 181). For a positive diagnosis, three of the following criteria must occur: (a) tolerance (a need for increasing amounts of the drug to achieve the desired effect); (b) withdrawal; (c) taking the substance in larger amounts or over a longer period than intended; (d) a persistent desire for or unsuccessful efforts to control use; (e) a great deal of time spent obtaining, using, or recovering from use of the substance; (f) important social, occupational, or recreational activities given up or reduced because of substance use; and (g) continued use despite recognition that a physical or psychological problem is caused or exacerbated by the substance. The DSM-IV description also states that tolerance, withdrawal, and compulsion are "usually" experienced while "craving," a strong subjective drive to take the substance, occurs in "most (if not all)" dependent individuals (American Psychiatric Association, 1994, p. 176). The differences between the British-based ICD-10 model of dependence and the American DSM-IV are significant, although subtle, reflecting differences in approach between American and British psychiatry. Room notes that British psychiatry has tended to take the view that social consequences do not belong in definitions of diseases or disorders (Room, 1998, p. 309).

Supporters of the dependence syndrome concept stress its flexibility; its inclusion of biological, psychological, and social factors' and its unwillingness to "assign a weight or special significance to any one factor or interaction" (Jaffe, 1992, p. 11). Indeed, as Room has pointed out, one of its most notable characteristics is that despite the sense of a unitary disorder conveyed by the term "substance dependence," no single affliction is described by this label (Room, 1998, p. 313). The diagnostic criteria are disjunctive, meaning that meeting any three qualifies as dependence; thus one sufferer could have no symptoms in common with another. There are many possible ways of being dependent on a substance, and there are a large number of substances one could be dependent on in all these various ways. Moreover, there is no single criterion shared by all who are diagnosed as dependent. However, unlike Edwards and Gross's provisional syndrome, the diagnostic approach of the ICD-10 and DSM-IV assumes that diseases are either present or absent, rather than existing in degrees of strength or manifestation.

Critics of the dependence syndrome have regarded it as both too similar to and too divergent from the disease concept. For many social scientists the dependence syndrome is simply the disease model repackaged, with all its major assumptions retained (Moore, 1992). In a wide-ranging critique, Stan Shaw (1979) argues that the dependence syndrome was not developed because of empirical or theoretical advances in the field, but in order to reestablish medical authority over addiction in the face of challenges from psychology and the social sciences.

Others in the field, especially those in the United States, regard the dependence syndrome as too vague about addiction as a primary and independent disease defined by specific and predictable symptoms. Norman S. Miller argues that the shift in terminology from drug addiction to substance dependence obscures the centrality of "loss of control" as the fundamental component (1995, p. 20). The use of the term *dependence* is also confusing, Miller suggests, because it can also refer solely to the physiological processes of adaptation. In this sense it is possible for someone to be dependent on a drug, after medical treatment for pain for example, but not to demonstrate the psychological and behavioral criteria of addiction (Miller, 1995, pp. 17, 21). For Miller it is clear that addiction is located in the drug-seeking behavior of the addict and, in particular, in the loss of control over his behavior. This emphasis on psychological and behavioral criteria, such as compulsion and craving, opens up the possibility for a range of non-substance based dependencies, such as sexual compulsion, food addiction, and exercise addiction (Jaffe, 1992). It also reinforces the status of psychiatry as the medical specialty best able to understand and treat addiction and alcoholism.

Biopsychosocial models are another example of expanded and updated understandings of addiction that retain a commitment to the disease concept. Advocates underscore the inclusivity and multidimensionality of biospsychosocial models, specifically their recognition of biological, behavioral, cognitive, psychosocial, and sociocultural elements in the etiology of addiction (Wallace, 1993). According to John Wallace, acceptance of what he calls the biopsychosocial disease model has the potential to end the "ideological skirmishes" over models of addiction (1993, p. 85). But although the model refers to social and cultural aspects of addiction, in practice these tend to be understood in a rather narrow way as individual risk factors and harmful consequences; for example, the role of peer groups in promoting drug use and the impact of drug use on relationships (see Landry, 1993).

NEUROLOGICAL AND LEARNING APPROACHES

With advances in neuroscience and imaging technologies, research on drug actions in the brain has become prominent in addiction science. Neurological accounts of addiction focus on the changes in "brain reward systems" that occur with the development of compulsive drug use, while accepting dominant medical models of dependence (for example, DSM-IV criteria). According to George F. Koob and colleagues, all drugs of abuse increase levels of the neurotransmitter dopamine in neural pathways that control pleasure (also known as the *mesolimbic system*) (Koob et al., 1999). It is hypothesized that as dependence develops, these pathways, which evolved to reinforce behaviors necessary to survival such as eating and sex, are "hijacked" by "artificial drug rewards" (Schultz, 2000; Nesse & Berridge, 1997). The brain adapts to the presence of a drug, and synapses and circuits are remodeled, increasing the reinforcing effects of the drug.

Neurological accounts of addiction have contributed to the increasing importance placed on positive reinforcement, or drug reward, in the production and maintenance of compulsive drug use. One of the most persistent debates in drug research is whether people continue to use drugs primarily to alleviate withdrawal and other negative states or primarily to experience positive rewarding effects (Jaffe, 1992). Neural models tend to focus on positive rather than negative reinforcement, specifically the brain rewards produced by psychoactive drugs (Wise, 1988). But the idea that physical dependence—defined by the presence of withdrawal symptoms—is the *sine qua non* of genuine addictive disease has remained influential. For example, Harold E. Doweiko's medical textbook published in 1993 uses "a demonstrated withdrawal syndrome" as the criterion to indicate whether a user "actually is addicted to a chemical" (Doweiko, 1993, p. 8). The use of physiological change as the criteria for addiction reflects a belief that a genuine disease is a fundamentally biological entity that affects the organic functioning of the body. It is noteworthy that a medical journal article by A. Thomas McLellan and colleagues based its conclusion that drug dependence was "a chronic medical illness" on its similarity to diabetes, asthma, and hypertension, rather than comparing it with psychiatric conditions (McLellan et al., 2000).

The implications of neurological accounts of addiction vary in relation to the disease status of addiction. On one hand, they highlight objective biological changes in brain anatomy and function as the basis of dependence. Alan Leshner, former head of the U.S. National Institute on Drug Abuse

has argued that it is crucial to recognize addiction as a brain disease because there are observable differences between "the addicted brain" and "the non-addicted brain" (Leshner, 1996; 1999). According to Steven Hyman, the dopamine model of drug action suggests that addiction is a disease of learning and memory, based on the brain recording powerful but pathological associations between drug use and pleasure. The role of memory explains why addiction is a "recalcitrant, chronic and relapsing condition" (Hyman, 2005, p. 1414). On the other hand, the neurological processes involved in drug addiction are the same as those involved in other forms of learning and memory. This suggests that addiction is not necessarily a disease but rather a form of learned behavior like any other. The understanding of addiction as learned behavior is one that has a long history in behavioral psychology.

ADDICTION AS LEARNED BEHAVIOR

The learning model found in psychology offers an alternative to disease conceptions because it does not classify deviant or harmful behavior as different from "normal" behavior. It views addiction and alcoholism as learned behavioral disorders that have been acquired and maintained in the same way as other repetitive, habitual, and recurring patterns of conduct (Lindstrom, 1992). Rather than a qualitatively different state from normal drinking, alcoholism is an extreme on a continuum of drinking behavior. Treatment aims to teach alternatives to destructive and antisocial habits, assuming that the alcoholic's "loss of control" is an acquired pattern of consumption that can be changed, rather than a symptom of a disease. Experimental research, which demonstrated that alcoholics' drinking was influenced by expectancy (whether they believed a drink contained alcohol) as well as studies that suggested alcoholics could drink moderately without relapsing, supported this challenge to "loss of control" as the central feature of alcoholism (Marlatt, 1978; Sobell & Sobell, 1978; Fingarette, 1988). However, the evidence supporting controlled drinking as a viable treatment goal for alcoholics has been contested (Sobell & Sobell, 1995).

In his learning-based model, Jim Orford (2001) examines how a strong attachment to an "appetitive behavior" is acquired, resulting in "unmanageable and excessive consumption." His model emphasizes the opposing psychological, social, and moral forces that are at play in the development of excessive behavior (whether it be drinking or drug use, eating, sex, or gambling). These oppositional forces can be summarized as restraint versus inclination, incentives versus disincentives, and conformity versus deviance. Thus it is not simply attachment, but conflict over attachment, that defines addiction. According to Orford, addictive behavior actually consists of a person's reactions to having developed a costly appetite and his or her response to the negative reactions of others. In his view, giving up an addiction is a naturally occurring process that begins with a personal decision, a decision triggered by the increasing accumulation of costs and conflict produced by the excessive behavior.

ALCOHOLICS ANONYMOUS: DISEASE OF THE SELF

As well as scientific and clinical expertise, the everyday "techniques of sobriety" developed by Alcoholics Anonymous (AA) and other twelve-step fellowships have had a profound impact on public understandings of addiction (Valverde, 1998). AA played a large role in spreading the idea of alcoholism/addiction as a disease, and the twelve-step approach to recovery is incorporated into many drug and alcohol treatment programs (Kurtz, 2002). Its first step, which requires the alcoholic to admit his or her powerlessness over alcohol, is consistent with the medical concept of "loss of control." However, the AA notion of alcoholism as a disease is not medical in a technical or scientific sense. Although it defines alcoholism as a progressive and incurable disease, it stresses the spiritual nature of the alcoholic's disorder and the crucial role of moral growth in recovery (Kurtz, 2002; Keane, 2002). Not surprisingly, the AA notion of disease is dismissed by some researchers as a vague formulation "unsupported either by clinical evidence or research findings" (Johns, 1990, p. 13). However, this fails to recognize that twelve-step models of addiction and alcoholism aim to represent the experience of disorder and despair from the sufferer's perspective, rather than conform to standards of scientific rigor.

It is the connection made between a disordered body and a disordered self that gives the notion of addictive disease, popularized by AA, its explanatory and descriptive power. On one hand, it

regards alcoholism (or addiction) as a bio-medical disease with specific predictable symptoms and a predictable natural course (Nowinski & Baker, 1992, p. xvii). But its symptoms, physical and behavioral, are nourished by a profound spiritual malaise. Self-pity, self-loathing, self-centeredness, and the absence of hope are viewed as the bedrock of the addict's existence but at the same time the addict is labeled as the victim of a physical disorder (Milhorn, 1994, pp. 32–42). The idea of a physiological anomaly that marks the addicted body is also used in a characteristically metaphorical manner to construct the addict as inherently and unchangeably different from "normal drinkers." Thus in AA the disease becomes the basis of a social identity that remains in place even if the alcoholic has achieved decades of sobriety.

MEDICAL DOMINANCE AND ITS CRITICS

Despite the success of self-help movements and the contributions of the psychological and social sciences, twenty-first-century alcohol and drug studies are marked by medical dominance. Alcohol and drug problems are seen as fundamentally biomedical issues, albeit issues with important psychological and social dimensions. In the United States biomedical research receives by far the greatest amount of the public funding in the alcohol field, and its dominance over areas like epidemiology and prevention is increasing (Midianik, 2006). Although the dependence syndrome model eschews the term *disease*, it is based on clinical observation of patients and sees the treatment of alcoholism and drug addiction as the responsibility of clinical medicine.

Social scientists have challenged medical perspectives on drug and alcohol use, pointing out the limitations of theories based on the small minority of drug users who seek treatment or medical care. Anthropologist David Moore argues that most drug use occurs in nonclinical populations and that it is unclear whether clinically defined dependence is applicable to community settings (1992, p. 462). He found that the notion of dependence as "a measurable psychobiological 'it'" made little explanatory sense when applied to the group of young amphetamine users he studied, whose drug use was best understood as part of the fluid and ongoing social action of their lives, and which increased and decreased in relation to cultural, social and economic aspects (Moore, 1992, pp. 484–486). Another question raised by social researchers is the cross-cultural applicability of the models of addiction and alcoholism developed in the West and based on Western understandings of selfhood and identity (Room, 1985; Alasuutari, 1992; Room et al., 1996).

While social scientific research on addiction is often not directly engaged with treatment design, in 2008 Peter Adams proposed a social model of addiction with an explicit application to the provision of drug and alcohol services. According to Adams, dominant views of addiction, including both the medical, psychological, and biopsychosocial, operate within a "particle paradigm." That is, they focus on the person suffering from the disorder as a discrete individual. He argues that a shift to a social paradigm, which understands addiction as a social event and sees people in terms of the nature of their relationships with others, opens up new opportunities for effective intervention.

Adams replaces the model of "an addiction" with the concept of an addictive system, a multilayered network of relationships that includes the addictive relationship between a member of the system and a substance. Other members of the system include immediate intimates, friends, colleagues, and community residents. This network becomes fragmented and unbalanced as the addictive relationship grows in strength, thus one-on-one counseling will have limited success unless there is reconstruction of the person's connections with other people and activities.

As Adams points out, paradigms of addiction can have concrete consequences; for example, in most community addiction services, practitioners see clients in small offices that are not suitable for meeting more than two people at a time, because they assume that the individual is the focus of treatment (Adams, 2008, p. 244). The conceptualization of addiction and alcoholism as a disease promotes abstinence as a universal treatment goal, while the dependence syndrome model suggests that the appropriateness of controlled drinking as a goal depends on the severity of dependence. While the process of medicalization has cemented the role of professional expertise in addiction treatment, self-help movements that value lay knowledge produced through firsthand experience of the disease continue to flourish. In most U.S. treatment programs, professional medical and

psychological services are combined with group therapies based on AA practice and ideals of fellowship (Yalisove, 1998). While it is useful to consider different models in their abstract conceptual form, in practice they are frequently combined in a pragmatic way, even when their assumptions may seem incompatible or contradictory.

See also **Addiction: Concepts and Definitions.**

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MONEY LAUNDERING. Obtaining the proceeds of crime has generally been but the first step for profit-motivated criminals. The use of those often has required a second step, whether it be to convert the money into form usable form for licit or illicit purposes, disguise its origins, avoid tax consequences, or make it possible to transport. As the quantity of money to be derived from illegal activity increases, the "laundering" of that money becomes more necessary with the internationalization of commerce, parallel markets, and increased technology. Money laundering has become more sophisticated as a consequence.

The International Financial Action Task Force, convened in 1989 by the G-8 Economic Summit, defines money laundering as "the process by which one conceals the existence, illegal source, or illegal use of the crime proceeds to make those proceeds appear legitimately derived." There are three steps to laundering funds: introducing the proceeds of

criminal activity into the legitimate economy (commonly referred to as "placement"); engaging in financial transactions designed to limit the ability to trace the funds (commonly referred to as "layering"); and making the funds available for use (commonly referred to as "integration").

In fact, depending on the objectives of individual criminals as far as convenience and security are concerned, the laundering process can be effected with as few as one and as many as a dozen discrete steps. In its most familiar form, hundreds of thousands of dollars in drug proceeds are taken to a financial institution and exchanged for a cashier's check, which the trafficker can carry around (or out of the country) with much less suspicion than suitcases full of cash. A slightly more involved scenario entails taking the same cash to the same bank, where it is deposited into an account and then sent by wire transfer to a bank in a foreign country, probably a jurisdiction renowned for the relative secrecy it affords customers like the hypothetical drug dealer.

In even more elaborate schemes, the same funds are wire-transferred around a circuit of accounts in different countries bearing the names of legitimate businesses. After the transfer reaches its final destination abroad, the owner in the United States arranges a sham transaction to bring the funds back into this country, often as the proceeds of a purported loan. There are literally countless varieties of laundering schemes, limited only by the imaginations of criminals and a more widespread impatience with transferring one's funds too far away.

Traditionally money laundering was conducted by the same individuals who committed the underlying criminal activity. Today, the sophistication of the process has given rise to the professional money launderer. But as money laundering has become more invaluable for criminals and criminal networks, governments have increasingly come to see the process as a potential vulnerability in the business of crime and have increasingly sought to curtail and prosecute it.

The United States began its legislative efforts to crackdown on money laundering in 1970 by requiring the reporting of cash transactions as part of the Bank Secrecy Act. As now modified, $10,000 in cash deposited in a financial institution or paid to a business will trigger the reporting requirements by the recipient of the funds. And with the Money Laundering Control Act of 1986, codified as 18 USC 1956 and 1957, Congress made it a crime to move certain illegally obtained funds through the commercial or banking system. Enforcement of anti-money laundering legislation was not only accomplished through the traditional penalties of incarceration and fines but also enhanced with powerful forfeiture remedies. Finally, since 1988 federal legislation has required banks to report "suspicious transactions." Individual states have sought to control money laundering with their own statutory and regulatory schemes. Internationally, the Financial Action Task Force and Interpol have approved resolutions, protocols, and recommendations calling for nations to pass legislation that would make money laundering a crime; require reporting of suspicious transactions; permit forfeiture; and allow extradition in money laundering cases.

U.S. anti-laundering legislation is complex and often controversial but what is perhaps most remarkable is the fundamental change in enforcement policy it represents, wrought by the requirement that non-law enforcement entities be compelled to engage in the systematic reporting of potential illegal activity. As a result, compliance programs requiring the recipient of funds to know its customer's business and to establish baselines from which suspicious activities can be identified are now the norm. For better or for worse, money laundering has brought the private world of commerce into the public field of law enforcement.

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RONALD GOLDSTOCK

MONITORING THE FUTURE. The use of illegal drugs by large numbers of young people in the United States became an issue of considerable concern during the late 1960s and

early 1970s. At that time, there were few accurate data available to assess the extent of use on a national basis. In 1975, psychologists Lloyd Johnston and Jerald Bachman of the University of Michigan initiated *Monitoring the Future: An Ongoing Study of the Lifestyles and Values of Youth*, which was intended to address this lack of information.

One of the major purposes of the study was (and is) to develop an accurate picture of the nature and extent of drug use among young people. An accurate assessment of the amount and extent of illicit drug use in this group is a prerequisite for rational policy making. Reliable and valid data on prevalence are necessary to determine an appropriate allocation of resources and to prevent or correct misconceptions. Reliable and valid data on trends allow for early detection of emerging problems and make it possible to assess the impact of external events, including historical events and deliberate policy changes.

In addition, the study was designed to monitor factors that might help explain the observed changes in drug use—that is, it was intended to serve both an epidemiological function (to learn how many young people use drugs) and an etiological function (to study why young people use drugs). The factors measured included attitudes toward drugs; peer norms and behaviors in regard to drugs; beliefs about the dangers of drugs; perceived availability of drugs; religious attitudes; and various lifestyle factors. The monitoring of these factors has among other things provided the country with valuable information. A particular contribution has been to help address a central policymaking question in the nation's war on drugs: the relative importance of supply versus demand factors in bringing about some of the observed changes in drug use.

STUDY DESIGN

The core feature of the design is an annual survey of each new high school senior class, beginning with the class of 1975. Each year approximately sixteen thousand seniors are surveyed in approximately 135 public and private high schools that have been scientifically selected to provide an accurate, representative cross-section of high school seniors throughout the coterminous United States. Data are collected following standardized procedures via closed-ended questionnaires administered in classrooms by University of Michigan representatives and their assistants.

In 1991 the project was expanded to include nationally representative samples of students from the eighth and tenth grades as well as from the twelfth grade. Each year, approximately eighteen thousand eighth-graders and sixteen thousand tenth-graders are surveyed, using procedures similar to those used in the twelfth-grade surveys.

One limitation of the design is that it does not include in the target population the young men and women who drop out of high school before graduation, and who make up between 15 and 20 percent of each age group nationally, according to U.S. Census statistics. The omission of high school dropouts does introduce biases in the estimation of certain characteristics of the entire age group, but because the dropouts are a relatively small proportion of the entire group the bias due to their omission is small. Because relatively few adolescents drop out before the end of tenth grade, the bias is particularly small for the eighth- and tenth-graders. It should also be noted that because any bias resulting from exclusion of the dropouts usually remains constant from year to year, the exclusion of dropouts should introduce little or no bias in estimates of change or trends.

An issue that is relevant to the study of such sensitive behaviors as drug use is the extent to which respondents will answer honestly. Considerable inferential evidence suggests that the procedures used in this study produce largely valid data. This evidence includes the following points: Large proportions of respondents report using illegal substances; various drugs exhibit trends in different ways over time; there are very few missing data in response to questions on drug use, even though respondents are instructed not to answer questions they would prefer not to answer; the high correlations with such other behaviors as grades, delinquency, religious attitudes, and truancy indicate a high degree of construct validity; a high degree of consistency can be noted over time in individuals' reports (that is, the responses are reliable); and other factors that are discussed in detail elsewhere (see Johnston, O'Malley, Bachman & Schulenberg, 2007; O'Malley, Bachman & Johnston, 1983).

	(Percent who used in last twelve months)																				
	1975	1980	1985	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Any Illicit Drug[a]																					
8th Grade	—	—	—	—	11.3	12.9	15.1	18.5	21.4	23.6	22.1	21.0	20.5	19.5	19.5	17.7	16.1	15.2	15.5	14.8	13.2
10th Grade	—	—	—	—	21.4	20.4	24.7	30.0	33.3	37.5	38.5	35.0	35.9	36.4	37.2	34.8	32.0	31.1	29.8	28.7	28.1
12th Grade	45.0	53.1	46.3	32.5	29.4	27.1	31.0	35.8	39.0	40.2	42.4	41.4	42.1	40.9	41.4	41.0	39.3	38.8	38.4	36.5	35.9
Any Illicit Drug Other Than Marijuana																					
8th Grade	—	—	—	—	8.4	9.3	10.4	11.3	12.6	13.1	11.8	11.0	10.5	10.2‡	10.8	8.8	8.8	7.9	8.1	7.7	7.0
10th Grade	—	—	—	—	12.2	12.3	13.9	15.2	17.5	18.4	18.2	16.6	16.7	16.7‡	17.9	15.7	13.8	13.5	12.9	12.7	13.1
12th Grade	26.2	30.4	27.4	17.9	16.2	14.9	17.1	18.0	19.4	19.8	20.7	20.2	20.7	20.4‡	21.6	20.9	19.8	20.5	19.7	19.2	18.5
Marijuana/Hashish																					
8th Grade	—	—	—	—	6.2	7.2	9.2	13.0	15.8	18.3	17.7	16.9	16.5	15.6	15.4	14.6	12.8	11.8	12.2	11.7	10.3
10th Grade	—	—	—	—	16.5	15.2	19.2	25.2	28.7	33.6	34.8	31.1	32.1	32.2	32.7	30.3	28.2	27.5	26.6	25.2	24.6
12th Grade	40.0	48.8	40.6	27.0	23.9	21.9	26.0	30.7	34.7	35.8	38.5	37.5	37.8	36.5	37.0	36.2	34.9	34.3	33.6	31.5	31.7
Inhalants																					
8th Grade	—	—	—	—	9.0	9.5	11.0	11.7	12.8	12.2	11.8	11.1	10.3	9.4	9.1	7.7	8.7	9.6	9.5	9.1	8.3
10th Grade	—	—	—	—	7.1	7.5	8.4	9.1	9.6	9.5	8.7	8.0	7.2	7.3	6.6	5.8	5.4	5.9	6.0	6.5	6.6
12th Grade	—	4.6	5.7	6.9	6.6	6.2	7.0	7.7	8.0	7.6	6.7	6.2	5.6	5.9	4.5	4.5	3.9	4.2	5.0	4.5	3.7
LSD																					
8th Grade	—	—	—	—	1.7	2.1	2.3	2.4	3.2	3.5	3.2	2.8	2.4	2.4	2.2	1.5	1.3	1.1	1.2	0.9	1.1
10th Grade	—	—	—	—	3.7	4.0	4.2	5.2	6.5	6.9	6.7	5.9	6.0	5.1	4.1	2.6	1.7	1.6	1.5	1.7	1.9
12th Grade	7.2	6.5	4.4	5.4	5.2	5.6	6.8	6.9	8.4	8.8	8.4	7.6	8.1	6.6	6.6	3.5	1.9	2.2	1.8	1.7	2.1
MDMA (Ecstasy)																					
8th Grade	—	—	—	—	—	—	—	—	—	2.3	2.3	1.8	1.7	3.1	3.5	2.9	2.1	1.7	1.7	1.4	1.5
10th Grade	—	—	—	—	—	—	—	—	—	4.6	3.9	3.3	4.4	5.4	6.2	4.9	3.0	2.4	2.6	2.8	3.5
12th Grade	—	—	—	—	—	—	—	—	—	4.6	4.0	3.6	5.6	8.2	9.2	7.4	4.5	4.0	3.0	4.1	4.5
Cocaine																					
8th Grade	—	—	—	—	1.1	1.5	1.7	2.1	2.6	3.0	2.8	3.1	2.7	2.6	2.5	2.3	2.2	2.0	2.2	2.0	2.0
10th Grade	—	—	—	—	2.2	1.9	2.1	2.8	3.5	4.2	4.7	4.7	4.9	4.4	3.6	4.0	3.3	3.7	3.5	3.2	3.4
12th Grade	5.6	12.3	13.1	5.3	3.5	3.1	3.3	3.6	4.0	4.9	5.5	5.7	6.2	5.0	4.8	5.0	4.8	5.3	5.1	5.7	5.2
Crack Cocaine																					
8th Grade	—	—	—	—	0.7	0.9	1.0	1.3	1.6	1.8	1.7	2.1	1.8	1.8	1.7	1.6	1.6	1.3	1.4	1.3	1.3
10th Grade	—	—	—	—	0.9	0.9	1.1	1.4	1.8	2.1	2.2	2.5	2.4	2.2	1.8	2.3	1.6	1.7	1.7	1.3	1.3
2th Grade	—	—	—	1.9	1.5	1.5	1.5	1.9	2.1	2.1	2.4	2.5	2.7	2.2	2.1	2.3	2.2	2.3	1.9	2.1	1.9

Note: See Johnston, O'Malley, Bachman, & Schulenberg (2007) for more specific details about measures.
[a]Use of "any illicit drugs" includes any use of marijuana, hallucinogens, cocaine, or heroin, or any non-medical use of other opiates (12th only), amphetamines, barbiturates (12th only), or tranquilizers.
[b]In 1982, the question about amphetamine use was revised; the prevalence rate declined as a result.
[c]In 1993, the question about alcohol use was revised; the prevalence rate declined as a result.

Table 1. Trends in annual prevalence of use of various drugs among eighth, tenth, and twelfth graders. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

	(Percent who used in last twelve months)																				
	1975	1980	1985	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Heroin																					
8th Grade	—	—	—	—	0.7	0.7	0.7	1.2	1.4	1.6	1.3	1.3	1.4	1.1	1.0	0.9	0.9	1.0	0.8	0.8	0.8
10th Grade	—	—	—	—	0.5	0.6	0.7	0.9	1.1	1.2	1.4	1.4	1.4	1.4	0.9	1.1	0.7	0.9	0.9	0.9	0.8
12th Grade	1.0	0.5	0.6	0.5	0.4	0.6	0.5	0.6	1.1	1.0	1.2	1.0	1.1	1.5	0.9	1.0	0.8	0.9	0.8	0.8	0.9
Other Narcotics																					
8th Grade	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10th Grade	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
12th Grade	5.7	6.3	5.9	4.5	3.5	3.3	3.6	3.8	4.7	5.4	6.2	6.3	6.7	7.0	6.7‡	9.4	9.3	9.5	9.0	9.0	9.2
Amphetamines[b]																					
8th Grade	—	—	—	—	6.2	6.5	7.2	7.9	8.7	9.1	8.1	7.2	6.9	6.5	6.7	5.5	5.5	4.9	4.9	4.7	4.2
10th Grade	—	—	—	—	8.2	8.2	9.6	10.2	11.9	12.4	12.1	10.7	10.4	11.1	11.7	10.7	9.0	8.5	7.8	7.9	8.0
12th Grade	16.2	20.8	15.8	9.1	8.2	7.1	8.4	9.4	9.3	9.5	10.2	10.1	10.2	10.5	10.9	11.1	9.9	10.0	8.6	8.1	7.5
Barbiturates																					
8th Grade	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10th Grade	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
12th Grade	10.7	6.8	4.6	3.4	3.4	2.8	3.4	4.1	4.7	4.9	5.1	5.5	5.8	6.2	5.7	6.7	6.0	6.5	7.2	6.6	6.2
Tranquilizers																					
8th Grade	—	—	—	—	1.8	2.0	2.1	2.4	2.7	3.3	2.9	2.6	2.5	2.6‡	2.8	2.6	2.7	2.5	2.8	2.6	2.4
10th Grade	—	—	—	—	3.2	3.5	3.3	3.3	4.0	4.6	4.9	5.1	5.4	5.6‡	7.3	6.3	5.3	5.1	4.8	5.2	5.3
12th Grade	10.6	8.7	6.1	3.5	3.6	2.8	3.5	3.7	4.4	4.6	4.7	5.5	5.8	5.7‡	6.9	7.7	6.7	7.3	6.8	6.6	6.2
Alcohol[c]																					
Any use																					
8th Grade	—	—	—	—	54.0	53.7	48.5	46.8	45.3	46.5	45.5	43.7	43.5	43.1	41.9	38.7	37.2	36.7	33.9	33.6	31.8
10th Grade	—	—	—	—	72.3	70.2	66.4	63.9	63.5	65.0	65.2	62.7	63.7	65.3	63.5	60.0	59.3	58.2	56.7	55.8	56.3
12th Grade	84.8	87.9	85.6	80.6	77.7	76.8	74.4	73.0	73.7	72.5	74.8	74.3	73.8	73.2	73.3	71.5	70.1	70.6	68.6	66.5	66.4

Note: See Johnston, O'Malley, Bachman, & Schulenberg (2007) for more specific details about measures.
[a]Use of "any illicit drugs" includes any use of marijuana, hallucinogens, cocaine, or heroin, or any non-medical use of other opiates (12th only), amphetamines, barbiturates (12th only), or tranquilizers.
[b]In 1982, the question about amphetamine use was revised; the prevalence rate declined as a result.
[c]In 1993, the question about alcohol use was revised; the prevalence rate declined as a result.

Table 1 (continued). Trends in annual prevalence of use of various drugs among eighth, tenth, and twelfth graders. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

MAJOR FINDINGS

As a broad generalization, there were four periods of change in use of illicit drugs among twelfth-graders: (1) an increase between 1975 and about 1980; (2) more than a decade of decline from 1980 to the early 1990s; (3) an increase in the mid-1990s from 1991 or 1992 to about 1997; and (4) another decade of decline, from about 1997 to 2007. Some specific drugs followed differing patterns, but the overall pattern is as described. The early increase between 1975 and 1980 almost certainly continued a longer-term period of increase that began in the 1960s. The early increase and subsequent decline were not observed among eighth- and tenth-graders, because they had not been surveyed. The increase in the early and mid-1990s was observed; indeed, the eighth-graders were the first to show definite signs of an upturn. The subsequent decline from about 1997 to 2007 was also evident in eighth- and tenth-graders.

Illicit Drugs. Annual use of any illicit drug (that is, any use in the past twelve months) peaked among high school seniors in 1979, when more than half (54 percent) of all high school seniors reported having used at least one illicit drug. This peak occurred following a rise in the late 1970s—from 45 percent in 1975, when the first reliable national data were collected. By 1992, the proportion had fallen to 27 percent, half the peak rate.

The statistics for lifetime prevalence are also dramatic. In the peak year of 1981, 66 percent of the graduating class reported having used an illicit drug at some point in their lifetime. By 1992, that percentage was down by about one-third, to 41 percent.

Unfortunately, the numbers of young Americans involved in the use of illicit drugs increased substantially during the 1990s. After reaching a low of 27 percent in 1992, annual use among seniors was back up to 42 percent in 1997 (still well below the peak value of 54 percent); lifetime use was at 54 percent.

Increases were particularly sharp among the eighth- and tenth-graders. No data are available before 1991, so longer-term trends are not so clear. However, it is clear that there were significant increases in the 1990s. Among eighth-graders in 1991, 11 percent had used an illicit drug in the past twelve months; that figure increased to 22 percent by 1997 (and actually peaked in 1996 at 24 percent). Similarly, among tenth graders, annual use increased from 21 percent in 1991 to 39 percent in 1997.

In the fourth of the four phases of change, there were declines in use of illicit drugs in the decade between 1997 and 2007. Annual use in 2007 was at 13, 28, and 36 percent for eighth- tenth- and twelfth-graders, respectively. These figures are well below historic peaks, but still above the historic lows of 11, 20, and 27 percent, respectively.

Among the various illicit drugs, marijuana is the most prevalent. The use of marijuana, as indicated by its annual prevalence, peaked among high school seniors in 1979, when a majority (51 percent) reported that they had used it in the past twelve months. Usage steadily declined after that, reaching a low of 22 percent in 1992. The annual prevalence, thus cut by more than half, declined from one in two seniors in the class of 1979 to fewer than one in four seniors in the class of 1992. However, by 1997 the figure was back up to 39 percent, so that well over one in three seniors had used marijuana in the past twelve months. In 2007, the figure had declined to 32 percent, still well above the low of 22 percent.

A particularly striking trend in marijuana use occurred between 1975 and 1978, when the proportion of seniors who reported using marijuana on a daily or near-daily basis in the past thirty days increased from 6.0 percent to an unprecedented 10.7 percent. This figure subsequently came down by more than 80 percent and stood at 2.0 percent in 1992. By 1997 it was back to 5.8 percent, just about where it was in 1975; by 2007 it was down, but only slightly, to 5.1 percent.

Among eighth-graders, annual marijuana use almost tripled from 6.2 percent in 1991 to 18 percent in 1997. Among tenth-graders, annual marijuana use doubled between 1991 and 1997, from 17 percent to 35 percent. The figures for 2007 were 10 and 25 percent respectively, down considerably from the peak years, but still higher than the low points.

Never as common as marijuana, cocaine became the drug on which the most attention was focused during the mid-1980s, when the national concern about the drug epidemic was at its highest level. The concern with cocaine was well founded because this drug had not followed the general pattern of decline

in the early to mid-1980s. As with marijuana, the use of cocaine had increased substantially between 1975 and 1979; annual prevalence doubled from 5.6 percent to 12.0 percent. Several years followed during which there was little change, with annual prevalence reaching a peak of 13 percent in both 1985 and 1986. A period of decline then ensued during which annual use declined to 3.1 percent in 1992; this was the lowest value recorded since reliable data had begun to be collected in 1975. Unlike marijuana, which peaked in 1996 or 1997, cocaine use increased throughout the 1990s, and by 1999 annual cocaine among seniors had again doubled, reaching 6.2 percent. By 2007, the figure was down slightly to 5.2 percent.

These data refer to the use of any form of cocaine, including crack cocaine. Crack cocaine first appeared in the early 1980s and became a significant factor among the illicit drugs in the mid-1980s. It was first assessed on a national basis in 1986, and its annual prevalence among high school seniors at that time was recorded at a disturbingly high 4.1 percent. That first reading turned out to be a peak level, and the use of crack cocaine declined thereafter, reaching 1.5 percent in 1992. Like powder cocaine, crack cocaine use increased through the 1990s in all three grades, then declined through 2007, when annual prevalence was between 1 and 2 percent in each grade.

Although inhalants are not actually illicit drugs, they are sometimes used illicitly for the purpose of "getting high." This particular behavior is generally more often seen among younger students rather than among high school seniors. In 2007, for example, 3.7 percent of twelfth-graders reported using inhalants to get high at least once in the past twelve months, compared to 6.6 percent of tenth-graders and 8.3 percent of eighth-graders.

Use of inhalants did not follow the four-phase pattern of change seen for illicit drugs in general. Among twelfth-graders, the longer-term trend in the use of inhalants was slightly upward from its lowest level of 3.0 percent in 1976 (when it was first assessed), to a peak level of 8.0 percent in 1995, before declining to 3.7 percent in 2007. Thus the use of this class of substance did not show the general decline from 1980 to 1992. All three grades showed some increase in the early 1990s, with peak levels in 1995, and overall, some irregular decline since then. Hallucinogens are the other major class of illicit (or illicitly used) substances that did not evince declines in the late 1980s and the early 1990s. LSD (lysergic acid diethylamide) in particular is a very significant exception; its use hardly changed among high school seniors, remaining at an annual prevalence of about 5 percent from 1987 to 1991 after a period of some decline. Like marijuana however, there was an increase in the 1990s, reaching 8.8 percent in 1996, the highest level ever recorded. By 2007, use had declined substantially, to 2.1 percent. Very similar patterns of change were evident among eighth- and tenth-graders, albeit at lower levels.

Substances that generally showed declines during the period from the 1970s to the early 1990s include heroin, opiates other than heroin, amphetamines, sedative/barbiturates, and tranquilizers. All of these substances also showed an increase during the mid-1990s. The patterns diverged somewhat after about 1997; use of heroin, amphetamines, and tranquilizers declined, while the use of opiates other than heroin and sedative/barbiturates tended to hold level or increase. Indeed, the nonmedical use of prescription drugs emerged in the twenty-first century as a relatively larger part of the drug problem, in part because the use of street drugs had decreased. Two medications—Vicodin and OxyContin—were particularly susceptible to misuse, reaching annual prevalence rates of 9.6 and 5.2 percent, respectively, among twelfth graders in 2007.

In the late 1990s, some "club drugs" appeared on the drug scene. One in particular, MDMA (methylenedioxymethamphetamine, or "Ecstasy") showed substantial increases, reaching 9.2 percent annual prevalence among seniors in 2001. The corresponding figures for eighth- and tenth-graders were 3.5 percent and 6.2 percent. Use then dropped as sharply as it had increased for a few years before increasing again in 2006 and 2007; annual prevalence rates in 2007 were 1.5, 3.5, and 4.5 percent in grades eight, ten, and twelve.

Alcohol and Tobacco. The history of the use of the major licit drugs—alcohol and tobacco—is rather different from that of the use of most illicit drugs. One significant difference was the extent of the use of alcohol and tobacco. The daily use of cigarettes was far greater than the daily use of any

other substance. In 1997, a quarter (25 percent) of high school seniors had smoked one or more cigarettes per day in the past thirty days. Even among eighth-graders, one in eleven was a daily cigarette smoker (9 percent). About one in twenty-five (3.9 percent) seniors drank alcohol daily or almost daily. All other drugs were used on a daily basis by 0.3 percent or less of seniors.

Alcohol is used pervasively throughout Western societies both as a food (beverage) and as an intoxicant. MTF asks students on how many occasions in the past two weeks they had five or more drinks in a row. The assumption is that anyone drinking that much would likely become intoxicated. The prevalence of this measure generally follows the four-phase pattern of change but at a more muted level, particularly in the 1991–2007 interval. The range from low point to high point in that interval was 25 to 32 percent among twelfth-graders, 21 to 26 percent among tenth-graders, and 10 to 16 percent among eighth-graders. During the 1980s, this measure of heavy drinking declined significantly among twelfth-graders, from a high of 41 percent to a low of 32 percent. Some, though not all, of the decline is likely attributable to raises in the minimum drinking age that occurred among many states as a result of federal legislation. Although heavy drinking has been declining very slightly in the new millennium, in 2007 this behavior was still at levels that most would consider unacceptably high —one in four twelfth-graders, one in five tenth-graders, and one in ten eighth-graders.

Cigarette smoking followed the recent pattern of a rise in the early 1990s, then a decline after about 1997. Unlike heavy drinking, the changes were substantial. Thirty-day prevalence ranged from the high point in 1996 or 1997 to the low point in 2007, from 37 to 22 percent for twelfth-graders, 30 to 14 percent for tenth-graders, and 21 to 7 percent for eighth-graders. Clearly, there was considerable progress made in reducing smoking, but equally clearly, there remained much room for additional progress.

DEMOGRAPHIC DIFFERENCES

Drug use among several demographic groups is monitored in the surveys, including gender, four-year college plans, parental education (an indicator of socioeconomic status), geographical region, population density, and racial or ethnic identification.

Gender. By senior year, male adolescents are more likely than female adolescents to use most illicit drugs, and the differences tend to be largest at the higher frequency levels. In 2007, for example, 6.8 percent of male high school seniors reported that they were using marijuana daily versus 3.2 percent of female seniors. For many specific substances, there is little gender difference in use among eighth- and tenth-graders. Indeed, eighth-grade females generally have slightly higher rates than males of annual use of inhalants, amphetamines, and tranquilizers.

There are gender differences in the prevalence of occasions of heavy drinking among high school seniors (31 percent for male adolescents versus 22 percent for female adolescents in 2007); thus, as with heavy use of illicit drugs, heavy use of alcohol is more likely among male adolescents than it is among female adolescents. This gender difference is considerably smaller than the one obtained in 1975, when the figures were 49 percent and 26 percent, respectively. The narrowing of the difference is primarily attributable to the greater decrease in heavy drinking among male adolescents than among female adolescents. The current differences are smaller among the younger students; among 2007 tenth graders, 23 percent of boys reported heavy drinking compared to 20 percent of girls; the corresponding figures for eighth-graders were 10 percent for each. Again, the narrowing of earlier differences reflects greater decreases among male adolescents.

In general, there is not much difference between male and female students in cigarette use.

College-Bound versus Non-College-Bound. Non-college-bound students are more likely than college-bound students to use any of the licit or illicit drugs. More frequent use of the drug tends to show greater differences. For example, in 2006 5.3 percent of non-college-bound eighth-graders reported smoking marijuana daily compared to less than 1 percent of the college-bound; corresponding figures for tenth- and twelfth-graders were 9 percent versus 2 percent, and 9 percent versus 4 percent, respectively. Striking differences show up between college-bound and non-college-bound students in cigarette smoking rates. For example, smoking a half pack or more a day was

	(Percent who used daily in last thirty days)																				
	1975	1980	1985	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Marijuana/Hashish any daily use																					
8th Grade	—	—	—	—	0.2	0.2	0.4	0.7	0.8	1.5	1.1	1.1	1.4	1.3	1.3	1.2	1.0	0.8	1.0	1.0	0.8
10th Grade	—	—	—	—	0.8	0.8	1.0	2.2	2.8	3.5	3.7	3.6	3.8	3.8	4.5	3.9	3.6	3.2	3.1	2.8	2.8
12th Grade	6.0	9.1	4.9	2.2	2.0	1.9	2.4	3.6	4.6	4.9	5.8	5.6	6.0	6.0	5.8	6.0	6.0	5.6	5.0	5.0	5.1
Alcohol[a] any daily use																					
8th Grade	—	—	—	—	0.5	0.6	0.9	1.0	0.7	1.0	0.8	0.9	1.0	0.8	0.9	0.7	0.8	0.6	0.5	0.5	0.6
10th Grade	—	—	—	—	1.3	1.2	1.7	1.7	1.7	1.6	1.7	1.9	1.9	1.8	1.9	1.8	1.5	1.3	1.3	1.4	1.4
12th Grade	5.7	6.0	5.0	3.7	3.6	3.4	3.0	2.9	3.5	3.7	3.9	3.9	3.4	2.9	3.6	3.5	3.2	2.8	3.1	3.0	3.1
5+ drinks in a row in last 2 weeks																					
8th Grade	—	—	—	—	12.9	13.4	13.5	14.5	14.5	15.6	14.5	13.7	15.2	14.1	13.2	12.4	11.9	11.4	10.5	10.9	10.3
10th Grade	—	—	—	—	22.9	21.1	23.0	23.6	24.0	24.8	25.1	24.3	25.6	26.2	24.9	22.4	22.2	22.0	21.0	21.9	21.9
12th Grade	36.8	41.2	36.7	32.2	29.8	27.9	27.5	28.2	29.8	30.2	31.3	31.5	30.8	30.0	29.7	28.6	27.9	29.2	27.1	25.4	25.9
Cigarettes any daily use																					
8th Grade	—	—	—	—	7.2	7.0	8.3	8.8	9.3	10.4	9.0	8.8	8.1	7.4	5.5	5.1	4.5	4.4	4.0	4.0	3.0
10th Grade	—	—	—	—	12.6	12.3	14.2	14.6	16.3	18.3	18.0	15.8	15.9	14.0	12.2	10.1	8.9	8.3	7.5	7.6	7.2
12th Grade	26.9	21.3	19.5	19.1	18.5	17.2	19.0	19.4	21.6	22.2	24.6	22.4	23.1	20.6	19.0	16.9	15.8	15.6	13.6	12.2	12.3
1/2 pack+/day																					
8th Grade	—	—	—	—	3.1	2.9	3.5	3.6	3.4	4.3	3.5	3.6	3.3	2.8	2.3	2.1	1.8	1.7	1.7	1.5	1.1
10th Grade	—	—	—	—	6.5	6.0	7.0	7.6	8.3	9.4	8.6	7.9	7.6	6.2	5.5	4.4	4.1	3.3	3.1	3.3	2.7
12th Grade	17.9	14.3	12.5	11.3	10.7	10.0	10.9	11.2	12.4	13.0	14.3	12.6	13.2	11.3	10.3	9.1	8.4	8.0	6.9	5.9	5.7

Note: See Johnston, O'Malley, Bachman, & Schulenberg (2007) for more specific details about measures.
[a]In 1993, the question about alcohol use was revised slightly.

Table 2. Trends in prevalence of daily use of marijuana, alcohol, and cigarettes among eighth, tenth, and twelfth graders. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

more than five times more prevalent among the non-college-bound 2006 eighth-graders than among the college-bound (5.8 percent versus 1.1 percent). Among seniors, half a pack or more smoking was more than three times as prevalent among the non-college-bound, 13 percent versus 4 percent. (The greater ratio in the younger students is likely due to the presence of the eventual dropouts in the eighth and tenth grades, because dropouts tend to have higher rates of smoking than nondropouts.) Non-college-bound students are also more likely than their college-bound counterparts to report having had five or more drinks in a row in the past two weeks (33 percent versus 21 percent among tenth graders, for example).

Parental Education. Among high school seniors there is (perhaps surprisingly) rather little association between parental education and use of illicit drugs. There is somewhat more of an association among the lower grades, particularly among eighth-graders, with the lowest level or lower two levels having somewhat higher use rates than the others.

Geographical Region. Overall, use of illicit drugs does not vary dramatically by region. Some differences emerge at times; for example, cocaine use was particularly high in the West in the early 1980s, and ecstasy use first emerged in the Northeast. However, use of specific illicit drugs usually spreads to all regions and differences become slight. Both the South and the West tend to exhibit slightly lower rates of alcohol use than the Northeast and the North Central states. For example, in 2007 the prevalence of heavy-drinking occasions (that is, five or more drinks in a row on at least one occasion in the past two weeks) among the seniors was 30 percent and 29 percent in the Northeast and North Central states, respectively, compared with 25 percent and 21 percent in the South and the West. Cigarette smoking tends to be lowest in the West.

Population Density. As of 2007, the differences in high school seniors' use of illicit drugs by population density were quite small. This lack of large differences reflects the fact that illicit drug use has spread widely throughout the nation. One substance that has shown some significant difference by population density over time is the use of cocaine. The substantial increase in cocaine use in the late 1970s and the continuing high levels of use until the mid-1980s were primarily an urban phenomenon. The annual prevalence rates for cocaine were nearly twice as high among high school seniors in the large standard metropolitan statistical areas as they were for seniors in the more sparsely populated areas. Unlike illicit drugs, cigarette use does vary somewhat by population density. For example, among tenth-graders, daily use in 2007 was at 10 percent in non-metropolitan areas, compared to 6 percent in the largest metropolitan areas and 7 percent in other metropolitan areas.

Racial or Ethnic Identification. It is difficult to make definitive statements about even the larger minority groups such as African Americans and Hispanics because of the relatively small numbers who participate in the surveys. Even Hispanics, who constitute a large segment of the population in many areas, often cannot be accurately represented because there are many important subgroups among the several Hispanic groups (e.g., Mexican, Puerto Rican, Cuban, and Latin American, among others). Nevertheless, certain findings appear to be reliable.

Among high school seniors, African American students report less use of virtually all substances than do white students. Generally, African American students in eighth and tenth grades also report less use of most substances, although marijuana is an exception in the eighth grade, where white students report less use.

By senior year, Hispanic students report higher rates of cocaine and crack cocaine than white or African American students. These differences are stronger among eighth- and tenth-graders. And particularly among eighth-graders, Hispanic students tend to show the highest rates of use for some substances, including marijuana, tranquilizers, and cigarettes. In other words, in eighth grade, before most dropping out of school occurs, Hispanic students are relatively high in use of substances, while white students tend to have higher rates by twelfth grade. Very likely, the higher rates of dropping out of school observed among Hispanic adolescents (U.S. Dept. of Education, 2007) accounts for the shift in differences.

Some of these differences could be due to differential reporting biases, but J. M. Wallace and J. G. Bachman (1993) argue that this is unlikely to be an important part of the explanation.

FOLLOW-UP SURVEYS AFTER HIGH SCHOOL

The core of the MTF study is the annual surveys of secondary school students as described above. However, there is another vitally important part of the study—follow-up surveys by mail of a sample of each high school graduating class. By following members of each class, the study is able to distinguish among three types of changes that can occur, specifically, age, period, and cohort (or birth group) effects. Knowledge that changes in, for example, alcohol use, are age-related (and not period- or cohort-related), is highly informative in revealing what kinds of variables might explain the age-related changes. All three types of changes have been found in varying degrees for the various substances (O'Malley, Bachman & Johnston, 1988; Johnston O'Malley, Bachman & Schulenberg, 2007). By following individuals through their post-high school lives, the study can also assess the impact of life-course changes that occur, particularly changes in social roles and social environments. Major transitions include higher education, moving out of the parental home, full-time employment, military service, getting married (and divorced), and becoming a parent. All these transitions have been explored by the project investigators, and results reported in various publications, including two books (Bachman et al., 1997; 2002). A further benefit of the follow-up surveys is that one important segment of the population—college students—is available for monitoring.

In addition to providing basic epidemiologic information on prevalences, trends, and demographic differences, the Monitoring the Future study also contributes information on the reasons for the trends and differences. The study's demonstration that attitudes and beliefs affect drug-use trends (especially in the case of marijuana and cocaine) is particularly important (Bachman, Johnston & O'Malley, 1990, 1998; Johnston, O'Malley, Bachman & Schulenberg, 2007). By virtue of its cohort-sequential design, the study has been able to distinguish among the several possible types of competing changes associated with trends in use; specifically, age, period, and cohort (or birth group) effects. A variety of changes in the post-high school environments have been investigated. In addition, the study has been able to provide important data with which researchers could evaluate the effects of changes in the laws dealing with marijuana (Johnston O'Malley & Bachman, 1981) and alcohol (O'Malley & Wagenaar, 1991). All of these contributions have been vital in the continuing debates about policy regarding the use of licit and illicit drugs.

See also **Adolescents and Drug Use.**

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PATRICK M. O'MALLEY

MONOAMINE. A monoamine is an amine that has one organic substituent attached to the nitrogen atom (as RNH_2). Serotonin is such an amine, one that is functionally important in neurotransmission. Chemically, monoamines include the catecholamines (derived from tyrosine) and the indoleamines serotonin and melatonin (derived from the amino acid tryptophan). Acetylcholine also has only a single (but trimethylated) amine, while histamine (a diamine formed from histidine) stretches the condition only slightly. Neurotransmitters in this class share several properties—nanomolar concentrations/milligram protein; neurons (nerve cells) that contain thin, generally unmyelinated axons to many brain regions; and their receptors (except for the cholinergic nicotinic receptor and one of the ten or so subtypes of serotonin receptors) employ second-messenger coupled transduction. Monoamine neurotransmitters are often involved in the action of mind-altering drugs and have been well studied.

See also **Dopamine; Neurotransmitters.**

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FLOYD BLOOM

MOONSHINE. Moonshine (white lightning) is the colloquial term for illegally produced hard liquor—whiskey, rum, brandy, gin, and vodka. The term probably originated around 1785, when it was recorded in a British book on vulgar language—used to describe the white (clear) brandy that was smuggled to the coasts of Kent and Sussex in England. In the New World, moonshine was made in homemade stills, usually from corn, especially in rural areas in the southern United States—before, during, and after Prohibition—and continues to be made today. The ethanol (drinking alcohol) content is usually high, often approaching 80 percent (160 proof). First-run moonshine contains a number of impurities, some of which are toxic, so it is necessary to double- and triple-distill the liquor to purify it for drinking.

See also **Alcohol: History of Drinking (International); Alcohol: History of Drinking in the United States; Legal Regulation of Drugs and Alcohol; Still.**

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S. E. LUKAS

MORNING GLORY SEEDS. The seeds of the morning glory, genus *Ipomoea* of the family Convolvulaceae, contain many lysergic acid derivatives, particularly lysergic acid amide. The hallucinogenic properties of some of these derivatives are not

Figure 1. Morning glory. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

known. The seeds can be ingested whole; they can be ground and used to prepare a tea; or the active compound can be extracted using solvents. The seeds have also been used as a source of precursors for the synthesis of lysergic acid diethylamide (LSD). Since the seeds contain lysergic acid derivatives, people ingesting morning glory seeds may feel "different"; however, the experience is not identical to an LSD-type "trip," even though the seeds are marketed on the street as an LSD equivalent.

Although morning glory seeds are easy to purchase legally, many varieties (those sold by reputable garden-supply distributors) have been treated with insecticides, fungicides, and other toxic chemicals—as well as with compounds that will induce vomiting if the seeds are eaten.

See also **Hallucinogenic Plants; Mescaline.**

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R. N. PECHNICK

MORPHINE. Morphine is a major component of opium, a product of the poppy plant (*Papaver somniferum* or *P. album*). Named after Morpheus, the Greek god of sleep, morphine is a potent analgesic (painkiller) that is widely used for moderate-to-severe pain. Morphine is one of approximately twenty alkaloids in opium. It was first purified in 1806; by the mid-1800s, pure morphine was widely used in medicine. At approximately the same time, the hypodermic needle and syringe were developed, which permitted the injection of the drug under the skin (subcutaneous [SC]), into muscles (intramuscular [IM]), or directly into the veins (intravenous [IV]). Together, these routes of administration are termed parenteral. Injections provide rapid relief from pain and can be used in patients who are unable to take medications by mouth. These advantages led to the widespread use of morphine injections during the American Civil War (1861–1865). At that time, the intense euphoria and addictive potential of these agents following injections was not fully appreciated, leading to the addiction of many soldiers. Indeed, morphine was legal and was sold over the counter or through mail order houses. Since that time, a major objective of pharmaceutical companies has been to develop a nonaddictive analgesic with the potency of morphine.

PHYSICAL DEPENDENCE AND ADDICTION

The concepts of *physical dependence* and *addiction* were not clearly differentiated until the mid-twentieth century, and it is likely that most early addicts were attempting to prevent the onset of withdrawal symptoms. Physical dependence is a physiological response to continued dosing with the opiate. Addiction, by contrast, implies drug-seeking behaviors despite the negative consequences of taking the drug. In the early twenty-first century few patients become addicted to opiates despite the fact that with continued administration all will become physically dependent; this fact may reflect the improved understanding of the drugs plus the modern ability to take a patient off medications without precipitating withdrawal symptoms. Morphine produces a wide variety of actions, some desired and others not. The definition of a desired action and a side effect depends on the reason for using the drug. For example, such opiates as morphine can be used to treat diarrhea but their constipating actions are usually considered an undesirable side effect when they are used to treat pain. Clearly, the control of pain remains the most important use of morphine. Morphine and other opiates relieve pain without interfering with traditional sensations. Patients treated with morphine often report that the pain is still there but that it no longer hurts.

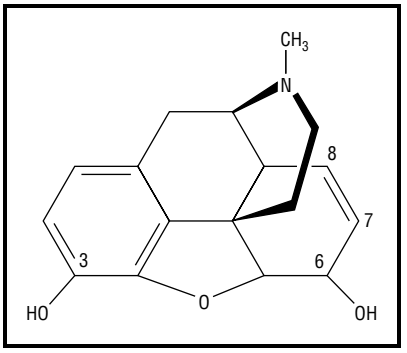

Figure 1. Chemical structure of morphine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

RECEPTORS

Morphine works through mu opiate receptors located within the brain and the spinal cord and along sensory nerves in the periphery. Morphine has a number of other actions as well. Its ability to constrict the pupil is one of the most widely recognized signs of opiate use. In addition, morphine produces sedation, and at higher doses morphine will depress respiration. Very high doses of morphine stop breathing entirely, a common occurrence in overdoses and the primary cause of death due to overdose. Morphine also has a major influence on the gastrointestinal tract, which is the basis for its antidiarrheal effect. Here, morphine decreases the motility of the stomach and intestine through local actions on the organs themselves, as well as through control systems located within the brain and spinal cord. Other systems can be affected as well. Morphine produces vasodilation, in which the peripheral blood vessels are relaxed. This effect can lead to significant drops in blood pressure when a person shifts from a lying to a standing position as the blood is pooled in the legs. This ability to pool blood in relaxed blood vessels can be used clinically to treat such conditions as acute pulmonary edema, an accumulation of fluid within the lungs, which occurs in acute myocardial infarctions (heart attacks). Increasing the capacity of the vascular system by relaxing the blood vessels permits the reabsorption of the lung fluid. Finally, morphine and such similar drugs, as codeine are also effective agents in the control of coughing. All of the effects of morphine can be easily reversed by antagonists, of which naloxone is the most widely used. Given alone, it has virtually no actions; however, low doses of naloxone are able to block or reverse all the actions of morphine described above.

ADMINISTRATION

Morphine is given either by mouth or by injection. Oral administration is associated with significant metabolism of the drug by the liver, explaining its lower potency as compared to that attained by injections. From three to six times more morphine must be taken by mouth to produce the same effects as an injected dose. Thus higher doses are needed when giving the drug orally. Morphine injections can be given either intramuscularly, subcutaneously, or intravenously. Continuous infusions are also common but their use is restricted to physicians who are expert in the treatment of pain.

Morphine has a relatively short effect in the body, around two hours, and it is usually given to patients every four to six hours and is extensively metabolized. In the late 1980s, it was discovered that one of the metabolites (breakdown products) of morphine, morphine-6β-glucuronide, is very potent, far more potent than morphine itself. The importance of this compound following a single dose of morphine is probably not great; however, with chronic dosing, the levels of morphine-6β-glucuronide in the blood may actually exceed those of morphine, so this metabolite may be responsible for many of morphine's actions. Since this metabolite is removed from the body by the kidneys, special care must be taken when giving morphine to patients with kidney problems. One common problem associated with morphine is nausea. Nausea does not occur in all patients and often is seen with one opiate but not others. Thus a patient unable to tolerate morphine may be able to receive therapy with methadone.

With chronic use, morphine has a progressively smaller effect, a phenomenon termed *tolerance*. To maintain a constant action it is necessary to increase the dose. Along with tolerance, morphine also produces physical dependence. Physical dependence (physiological dependence; neuroadaptation) develops as the body attempts to compensate for many of morphine's actions. As long as a person continues to receive the drug, no symptoms are noted. Abrupt cessation of the drug or the administration of an antagonist, such as naloxone or the related compound naltrexone, produces a constellation of symptoms and signs termed the *withdrawal syndrome*. Early symptoms include restlessness, tearing from the eyes and a runny nose, yawning, and sweating. As the syndrome progresses, one sees dilated pupils, sneezing, elevations

in heart rate and blood pressure, and gooseflesh (which is responsible for the term *cold turkey*). Cramping and abdominal pains are also common.

As mentioned above, physical dependence (or neuroadaptation) is a physiological response to repeated dosing with morphine and is seen in virtually all patients repeatedly given morphine or another opiate drug. Physical dependence, however, is distinguished from drug dependence or addiction, which is defined by drug-seeking behavior. While addiction is common among drug abusers, it is rare when morphine is used for appropriate medical conditions. The reasons for this difference were not clear as of 2008, and they remain a major issue in understanding and treating opiate addiction.

See also **Addiction: Concepts and Definitions; Diagnostic and Statistical Manual (DSM); Opiates/Opioids; Opioid Complications and Withdrawal.**

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MOTHERS AGAINST DRUNK DRIVING (MADD).

Mothers Against Drunk Driving (MADD) is a national organization that works to reduce drunk driving and to help the victims of drunk driving accidents. Many of MADD's members are volunteers who have personally suffered from the results of drunk driving.

MADD was founded by Candy Lightner, whose 13-year-old daughter, Cari, was killed by a drunk driver on May 3, 1980. Lightner was outraged to learn that only two days before the accident that killed her daughter, the driver had been released from jail, where he had been held for another hit-and-run drunk driving crash. Although he had been arrested for drunk driving several times before, he was still driving with a valid California license. Candy Lightner decided to begin a campaign to keep drunk drivers off the road so that other mothers would not have to suffer the anguish she was experiencing. On September 5 (Cari's birthday), 1980, MADD was originated.

Since then, MADD has evolved into an organization with millions of members and hundreds of local chapters across the United States. Chapters have also been started in Canada, Great Britain, New Zealand, and Australia. Membership is not restricted to mothers of victims or to the victims themselves. Everyone who is concerned about the drunk driving issue is welcome to join. Funding for the organization comes from membership dues and contributions. MADD also applies for and receives grants from federal and state governments and private organizations. Paid staff members are employed to provide leadership on the state and national levels. MADD is involved in three major kinds of activity: (1) advocacy for stricter drunk driving laws and better enforcement, (2) promotion of public awareness and educational programs, and (3) assistance to victims.

THE LEGISLATIVE AGENDA

According to MADD, drunk driving is a violent crime. One of its rallying slogans is "Murder by Car Is Still Murder!" Over the years, MADD members have worked to generate public support for passage of stricter drunk driving legislation, punitive sanctions, and more consistent enforcement measures aimed at deterring drunk driving. In the 1980s, intense lobbying efforts were undertaken for the passage of laws making 21 the minimum legal age for drinking (now in force in all 50 states). The group believes that this measure has saved thousands of young lives that would have been lost in drunk driving crashes.

MADD has also lobbied for changes in judicial procedures that would make the system more responsive to victims of drunk driving. For example, in many states victims had been barred from the courtroom during the trial of their own drunk driving cases because their testimony (or even their presence) might prejudice the jury. Because of the efforts of MADD and other groups, victims' rights bills have now been passed in all states. These ensure that victims will be notified about court hearings and, in most states, allowed to testify about the impact of the crime on their lives. Other lobbying efforts have sought to close legal loopholes that drunk drivers were using to avoid

punishment. For example, drivers might have refused to take a Breathalyzer or blood test for intoxication and were allowed to plead guilty to a lesser charge. In other cases, drivers were allowed to claim that despite their high blood alcohol content, their driving was not really impaired.

MADD has been instrumental in the passage of more than 1,000 tougher drunk driving laws that close these loopholes and institute other deterrent measures, such as mandatory jail sentences for drunk drivers. MADD also supports efforts to require offenders to undergo treatment for alcoholism and/or drug dependency, if this is deemed necessary.

PUBLIC AWARENESS AND EDUCATION

MADD is involved in various efforts to raise public awareness and concern about drunk driving. The National Candlelight Vigil of Remembrance and Hope is held in many locations each December, drawing victims together to give public testimony to the suffering that results from drunk driving. During the Red Ribbon: Tie One On for Safety campaign, which takes place between Thanksgiving and New Year's Day, MADD encourages citizens to attach a red ribbon to their car as a reminder to themselves and others to drive sober. MADD's well-known public awareness campaign of the past used the slogan, "Think . . . Don't Drink and Drive" in public-service announcements on radio and television and in print materials. A more recent campaign, "Keep It a Safe Summer (KISS)," emphasized the need for sobriety during recreational activities that involve driving, boating, and other activities that might pose a danger when under the influence of alcohol. MADD also provides curriculum materials for schools and each year sponsors a poster and essay contest for children on the subject of drunk driving.

ASSISTANCE TO VICTIMS

Programs that provide aid to victims of drunk driving crashes constitute the heart of MADD's mission. Support groups help victims share their pain with others who understand their feelings. MADD members send "We Care" cards to victims of recent crashes. Specially trained victim advocates offer a one-on-one personal relationship with victims, trying to respond to both their emotional and practical needs. Victims are briefed on their legal rights and on the judicial procedures relevant to their cases. They can call a toll-free number (1-800-GET MADD) for information and help in case of a crisis. MADD also offers death-notification training for police and specialized training for other community professionals, such as clergy and medical workers, who are called on to assist victims.

"20 × 2000"

Since the founding of MADD in 1980, the percentage of alcohol-related traffic fatalities has steadily decreased, from almost 60 percent to around 50 percent. In 1995, MADD established "20 × 2000," a program that sought to reduce that proportion by an additional 20 percent by the year 2000. Intensified efforts focused on more effective law enforcement, increased sanctions, and prevention programs that included education for youth and more responsible marketing and service practices in liquor establishments. The program coincided with federal laws tying state highway funding to passage of state legislation establishing zero tolerance laws aimed at drunk drivers. Because of its concerted efforts in changing the culture of how many Americans perceived drunk driving and its risks, MADD reached its "20 × 2000" goal three years early, when alcohol-related traffic fatalities fell to below 40 percent nationally by 1997.

See also **Blood Alcohol Concentration; Blood Alcohol Concentration, Measures of; Breathalyzer; Dramshop Liability Laws; Driving, Alcohol, and Drugs; Driving Under the Influence (DUI); Legal Regulation of Drugs and Alcohol; Minimum Drinking Age Laws; Psychomotor Effects of Alcohol and Drugs.**

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REVISED BY MATTHEW MAY (2009)

MOVIES. The use and abuse of substances may be observed in movies from virtually any genre, location, and era. One of the earliest examples of drug use in film is the 1906 French movie *Les Rêves d'un Fumeur d'Opium* (The Opium Smoker's Dream). Substances may play a minor role in a movie, serving to enhance a particular storyline or character. Alternatively, they may play a central role, representing aspects of use and abuse at the individual, community, or societal level. Although the portrayal of substances in movies may have a particular entertainment value, it is important to recognize that they may also shape a viewer's belief system and stereotypes about persons who use and abuse substances.

Research guided by social learning theory shows that "learning is achieved through not only direct experience but also through observation" (Stout et al., 2004, p. 544; see also Bandura, 2002). This suggests that viewer perceptions of persons who use and abuse alcohol and drugs can be directly influenced by the portrayal of substances in films. In a review of more than 50 movies, Cape (2003) found that both positive and negative stereotyping surround the use and abuse of substances. The major stereotypes include the tragic hero, rebellious free spirit, demonized addict/homicidal maniac, and humorous/comedic user. In addition to shaping beliefs, films can provide a historical context, helping the viewer to understand the broader culture and beliefs about substances during a particular time. This entry highlights some of the different genres of movies that portray the use and abuse of substances, the types of characters exemplifying the stereotypes outlined by Cape (2003), and the interplay between different genres of movies and the historical context.

DRAMAS

Dramas provide fictional accounts of the lifestyle or culture associated with substance use, varying significantly in their realism. They offer the viewer a unique perspective into buying and selling substances, the social contexts in which they are used, and their biopsychosocial consequences, exhibiting significant heterogeneity in realism and accuracy. Some of the earliest movies were influenced by an era of severe moralistic reasoning. For example, Dorothy Davenport produced *Human Wreckage* (Davenport & Wray, 1923), which served as a drug-prevention film following the morphine-related death of her husband Wallace Reid. In this film, drug use was associated with moral deficiency in a propaganda-like manner. It provided definitions of moral behavior in the midst of numerous Hollywood scandals. Such events and the emphasis on morality guided the architecture of the Production Code of the Motion Picture Industry (better known as the Hays Code) of the 1930s. This was an attempt by the Motion Picture Association of America to explicitly define what was acceptable in movies, with the ultimate goal of advancing proper or moral behavior. From the Hays Code emerged films that contained substances as a central theme, with a clear purpose of propaganda.

At a time when very little knowledge about substances existed, these movies helped warn parents and youth about the jeopardy of one's morality when using illicit substances. For example, the films *Reefer Madness* (Hirliman & Gasnier, 1936) and *Assassin of Youth* (Brown & Clifton, 1937) showed well-adjusted individuals having extreme and sensational reactions when high on marijuana. These films suggested that typical responses include insanity, suicidal behavior, and violence, and connected marijuana use with premarital sex and listening to jazz music, two societal taboos of the time. Similar portrayals of other drugs can be found in films of the same period, such as *Cocaine Fiends* (Kent & O'Connor, 1935). In *The Lost Weekend* (Brackett & Wilder, 1945), the main character engages in a weekend of binge drinking. Subsequent to his intoxication, he becomes involved in criminal activity and serves time as a patient in a psychiatric ward.

The Man with the Golden Arm (Preminger & Preminger), released in the 1950s, also illustrated themes similar to those of the early propaganda

films, highlighting the negative consequences of illicit drugs. This film opens with the release of the central character, Frankie Machine (played by Frank Sinatra), from prison, clean and sober from a heroin addiction. Upon returning home, he struggles in a social environment that challenges his sobriety, and he quickly succumbs to heroin use, illegal card dealing, and dodging the police. The insanity, violence, and deviant behavior of the characters in these films match the demonized addict/homicidal maniac stereotype. These films often had subtle or explicit intentions to educate and instill fear associated with using substances. A viewer of the early twenty-first century might find the portrayal of the substances to be humorous, given available knowledge on the actual effects of the substances.

A shift from bombarding the viewer with the harmful effects of substances to a more tolerant view occurred in the 1960s and 1970s, during an era of counterculture, experimentation, and political unrest. A complete breakdown in social functioning due to substance use was no longer the norm. Such films featured the tragic hero stereotype, with the main characters retaining likable qualities despite their struggles and poor choices associated with substances. For example, *Easy Rider* (Fonda & Hopper, 1969) showed the main characters Captain America (played by Peter Fonda) and Billy (Dennis Hopper) traveling across the United States in search of freedom and financial gain by selling drugs. On their journey, Captain America and Billy fight locals who view the "hippie" drug salesmen as a detriment to their communities. The viewer is led to sympathize with the protagonists, rather than feeling disdain toward their drug dealing. The broader social and political context of such films, intertwined with the Vietnam War, made them appealing to a wide audience.

Another important social and political shift occurred in the 1970s and 1980s, with the end of the Vietnam War and a growing body of scientific evidence on drugs becoming available. Nancy Reagan championed the "Just Say No" campaign, and the Drug Abuse Resistance Education (DARE) program was implemented. Zero tolerance policies and harsh drug laws began to be enforced. This change in knowledge and beliefs gave rise to a much different portrayal of substances. It is not clear to what extent these policies shaped the portrayal of substances in the movies, especially with a greater emphasis on artistic and creative directorship. However, this period marked a return to portraying substances negatively with much realism. For example, *Ulee's Gold* (Gowan & Nunez, 1997) illustrates the troubling consequences that drug use can have on an addict as well as his family and friends. It bears noting that Peter Fonda starred in this film as well as *Easy Rider*, providing a stark contrast between two cultural moments. The audience becomes witness to a character's severe detoxification and to the dangerous people who are often associated with the drug scene. *Trainspotting* (Macdonald & Boyle, 1996) portrays the dark side of heroin dependence, including severe withdrawal symptoms, hallucinations, drug seeking behaviors, overdose, relapse, and troubled social relationships. *Go* (Freeman & Liman, 1999) depicts a group of young friends who use and sell Ecstasy at rave parties. These friends must confront the realities associated with drug dealing, including threats of violence and the need to engage in high-risk behaviors.

Besides showing the consequences of movies, it is important to note that many dramas also focus on issues related to recovery and treatment. As in the other films discussed, these films also reflect the current knowledge and beliefs at the time they were filmed. For example, the earlier *Days of Wine and Roses* (Manulis & Edwards, 1962) shows the struggles associated with recovering from an addiction. The film illustrates a married couple's personal, social, and professional struggles associated with their alcohol dependence. Alcohol is portrayed as being a major contributor to reckless and dangerous behavior when the intoxicated wife nearly kills herself and the couple's child after accidentally setting a fire in the family's apartment. The film closes with the husband achieving sobriety through the assistance of Alcoholics Anonymous and attempting to persuade his wife to join him in the journey to recovery. This was the only treatment option of the time. A more recent film, *28 Days* (Topping & Thomas, 2000), shows a woman, Gwen Cummings (played by Sandra Bullock), forced to make a choice between jail or 28 days in a rehabilitation center after she gets in a car accident while driving drunk. She fulfills her sentence at a rehabilitation center, with the treatment

process involving the serenity prayer, a twelve-step program, and family therapy. Treatment and recovery films such as *28 Days* can have an impact on the way the viewer perceives people who seek help for their addiction. Hersey (2005) argues that this type of film may unrealistically portray individuals seeking treatment and the treatment process itself. The main characters tend to be white and upper-middle-class, and undergo treatment in expensive settings that are generally not reflective of typical treatment options, such as outpatient treatment.

COMEDIES

Although some films attempt to portray the negative consequences of substance abuse, many films take a different approach. That is, they glorify substance use and misuse using a comedic perspective. They tend to avoid showing the negative consequences of substance abuse or do so in a humorous way. Although the War on Drugs has had a lasting effect on the themes expressed in drug-related dramas, comedic films have more flexibility in their perspective and tone. Both the shift in societal perspective during the 1980s and current scientific data have illustrated the devastating physical consequences of narcotics such as cocaine, heroin, and opiates, making a comedy based on these substances unlikely. Comedic drug films tend to focus on the use of alcohol or marijuana, often distorting their true effects.

So-called stoner films center on the use of marijuana and typically have outlandish plots and humorous protagonists. Their titles often make explicit references to marijuana use, as evidenced by the films *Half Baked* (Simonds & Davis, 1998), *Dazed and Confused* (Daniel & Linklater, 1993), and *Up in Smoke* (Adler & Adler, 1978). *Half Baked*, like *Go*, features main characters involved in the drug-dealing business; unlike *Go*, however, the characters in *Half Baked* are never perceived to be in serious danger or trouble as a result of their involvement in this drug culture—despite a minor plot appearance from police and a greedy drug king. The hallucinations experienced by the characters in *Half Baked* are also quite different from those in more typical films with an antidrug message in that the *Half Baked* characters generally have fun and enjoy their humorous experiences while high.

Another common type of comedy portrays young characters eager to experiment with or use substances—partying. This genre of drug film typically involves using a large quantity of substances, especially alcohol, with kegs of beer and shots of hard liquor being commonplace. Parents are generally not main characters in these films as the majority of the film actually centers on the party and youth themselves. Much like stoner films, party films do not portray the negative consequences associated with substance use, or the consequences become a central point of the comedy. *National Lampoon's Animal House* (Reitman & Landis, 1978) is a classic party film. Such films frequently take place in a college, depicting the use of alcohol as a social lubricant and catalyst for many gags.

Comedic films often have characters that reflect the humorous/comedic user or rebellious free spirit stereotype. More times than not, the substance use or culture is the vehicle for humor. This is particularly evident when substances are a component of a party setting, as they tend to minimize any negative consequences associated with their use. A potential danger of this type of film, as suggested by social learning theory, is that the viewer misunderstands the actual consequences.

DOCUMENTARIES

Documentary or non-fiction movies are another means for portraying the use of alcohol and drugs. These movies allow the audience to view the experiences of an actual person or group of individuals rather than through a fictional account or storyline. For example, *Children Underground* (Belzberg & Belzberg, 2001) depicts the existence of impoverished Romanian youth who abuse inhalants and live in the subway system. The viewer learns about the consequences related to the youths' addiction to inhalants, including prostitution, stealing, begging, and other physical and mental health problems. The documentary *REHAB* (Okazaki & Okazaki, 2005) provides an insider's look into a 30-day rehabilitation facility for persons with various types of substance use disorders and histories. The people featured in this documentary share their struggles in recovery through anecdotes and day-to-day interactions during and after treatment. The documentary also highlights the challenges that individuals may face in their efforts to achieve and maintain sobriety.

Documentaries may lend themselves to a variety of stereotypes, depending on the viewpoint and story portrayed. In these examples, and many others, the tragic hero stereotype was exemplified. Although documentaries may attempt to depict true-life accounts of people or events, it is important to recognize that there is a fine line between an objective portrayal and propaganda. Beliefs about substances are arguably influenced by social, political, and moral values. Thus, documentaries may have an underlying motivation to advance a particular system of beliefs while maintaining a position of objectivity.

IN CONCLUSION

Tremendous diversity exists in the portrayal of alcohol and drug use in movies, including but not limited to the depiction of consequences, contexts surrounding use, and the extent to which use is sensationalized. The portrayal may be intended for purposes of entertainment. However, there are sometimes unintended consequences, such as advancing stereotypes about persons with substance use disorders and minimizing the actual risks of use, especially binge drinking. As alcohol and drugs are ubiquitous, particularly in American culture, the depiction of use and misuse can be expected to continue playing an important role in movies.

See also **Internet: Impact on Drug and Alcohol Use; Media; Music.**

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MPTP. MPTP is a neurotoxin that was accidentally produced during an illicit manufacturing process. To circumvent the laws regarding controlled drugs, a chemist attempted to synthesize a derivative of meperidine. By synthesizing a new derivative not specifically covered by the Controlled Substances Act and existing Drug Enforcement Agency laws and by synthesizing the drug and selling it within the same state, the chemist had hoped to profit while avoiding violation of the laws. This designer drug approach was being widely used to avoid prosecution for selling drugs of abuse—however, in this case a side product was also formed in this reaction, MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). People who bought this mixture on the street quickly developed a neurological syndrome virtually indistinguishable from Parkinson's disease. Initially the cause of this problem remained unknown. With intense investigation, the blame was placed on the side product in the reaction, MPTP. MPTP had long been used as an intermediate in chemical synthesis and was commercially available. The ability of MPTP to provoke a Parkinson-like syndrome helped explain a report from years ago of a chemist working with this compound suddenly developing a disease resembling Parkinson's.

The Parkinson-like syndrome is very similar to the symptoms originally described in Parkinson's disease. The most notable aspects of the syndrome are the marked cog-wheel rigidity of the muscles, along with a generalized decrease in movement usually associated with problems initiating the movement. Patients often have difficulty with such fine motor skills as writing; and with walking, which usually becomes a series of small, shuffling steps termed a "festinating gait"; their greatest problem is starting and stopping. Diminished blinking coupled with a limited facial expression can be very prominent and is termed "masked facies." In Parkinson's disease, patients also have a pill-rolling tremor and a tendency to fall because of problems with blood pressure and the reflexes important to maintaining posture.

Pathologically, Parkinson's disease is noted for a degeneration of pigmented nuclei within the brain, including the substantia nigra. The loss of the dopaminergic neurons in the substantia nigra that project to the part of the brain called the striatum is responsible for the motor problems; while the degeneration of other areas of the brain, including the locus ceruleus, are presumably responsible for the autonomic problems. The cause of Parkinson's disease is still not known; treatment is symptomatic. Early studies demonstrated the ability of anticholinergic medications to help with many of the motor symptoms, especially the tremor. However, the drug of choice in the early 2000s is L-dopa, a precursor of dopamine. Unlike dopamine, which does not traverse the blood-brain barrier, L-dopa is readily transported into the brain where it is taken up into neurons and converted to dopamine—thereby helping to reduce symptoms caused by loss of dopamine-containing neurons. Replacement of the dopamine can markedly limit the severity of the motor symptoms; however, the duration of this benefit is often limited to only about five years, presumably due to the continued progression of the disease.

MPTP does not bind to opioid receptors and it has no opioid activity, although it is a side product in the synthesis of a meperidine analog. When ingested, it is taken up into neurons containing a catecholamine transporter, greatly limiting the neurons affected. Once in the cell, the drug is converted by the enzyme monoamine oxidase (type B) in a series of steps to another compound, MPP+, which is believed to be responsible for its toxic actions. The need for the transporter to take up the toxin into the cells partially explains its selective toxicity within the brain. There, this drug destroys the same groups of pigmented catecholinergic neurons affected in Parkinson's disease, including the substantia nigra and the locus ceruleus. The greater sensitivity of pigmented neurons to the toxin is still not completely understood. One hypothesis has been put forward: The color in the neurons is due to the pigment melanin, which actively binds the toxin. Therefore, it has been suggested that this binding results in the accumulation of very high levels of the drug, which persist in the neurons for long periods of time, enhancing its toxicity.

Clinically, MPTP produces a syndrome virtually identical to that seen in Parkinson's disease; but Parkinson's is a progressive degenerative disease, which, over the period of many years, gradually leads to a variety of difficulties with thought and memory. It is not thought that MPTP produces a

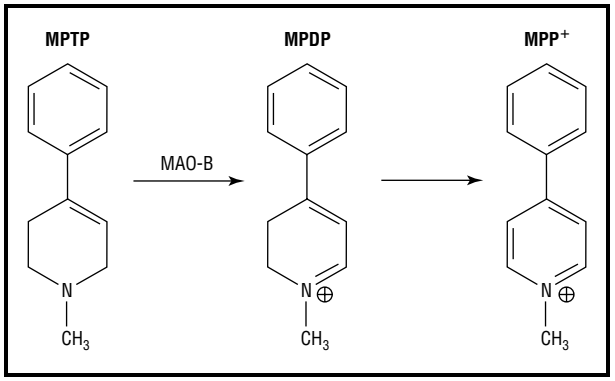

Figure 1. MPTP conversion to MPDP and MPP^+. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

similar global, diffuse loss of function. The marked similarity, though, has led to the speculation that Parkinson's may be due to exposure to a toxin similar to MPTP. Since the toxicity of MPTP depends on its conversion by type B monoamine oxidase (MAO-B), it was suggested that inhibition of this enzyme may prove beneficial. Selegiline is a selective MAO-B inhibitor, and early clinical trials suggested that the progression of Parkinson patients taking this medication may be slower than in the control groups. In the 1990s Selegiline was approved by the FDA to treat Parkinson's disease. In 2006 it was approved to treat depression.

See also **Controlled Substances Act of 1970; Meperidine; Receptor, Drug.**

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MULTIDOCTORING. Multidoctoring—also known as double-doctoring, doctor-shopping, or multisourcing—refers to the practice of utilizing more than one health-care provider or prescriber (e.g., a physician or mid-level practitioner, such as a nurse practitioner or physician assistant) as the source for medications or other medical services, without informing the individual practitioners of any medications already being prescribed. It typically refers more directly to obtaining scheduled drugs (or, more rarely, sexual performance enhancement medications) in quantities that would be difficult to obtain from one source. The medications involved are most commonly from the group considered to be "brain reward" or "euphoria producing" drugs. These drugs are considered to be potential drugs of abuse or addiction, and they generally have a value on the secondary, or "street," market. These medications produce an acute surge of dopamine from the midbrain (the ventral tegmental area [VTA] and nucleus accumbens) to the forebrain (the prefrontal cortex), which causes the brain-reward or euphoria effect. Since the mid-1990s, there has been a substantial increase in the abuse of controlled prescription drugs, as well as an attendant increase in concerns about the multisourcing of these drugs.

The classes of medications involved in multidoctoring include: (1) sedative hypnotics (benzodiazepines, barbiturates, and other sedative-like drugs), (2) the opioid and opiate analgesics, and (3) the psycho-stimulants. These drugs are typically covered under the Federal Controlled Substances Act and are scheduled in descending order of abuse potential as CII, CIII, CIV, or CV medications. A few nonscheduled drugs are also the focus of multisourcing activity, including carisoprodol (Soma), tramadol (Ultram), butalbital/acetaminophen (Fioricet), and (as mentioned above) the sexual performance enhancement or erectile dysfunction medications. Each of these medications has a street value that exceeds its pharmacy value, and this value is proportionally related to the amount of and rapidity of the euphoria-producing effect of each drug.

Individuals who engage in multidoctoring or multisourcing behavior may obtain the medications for their own use, or they may intend to resell the drugs on the street. People who seek controlled drugs for the purpose of abuse or resale are often very convincing in their appeals, and they can therefore often get physicians or mid-level practitioners to prescribe the drugs requested. To maintain their drug supply, addicted patients typically pressure the physician for more medication,

pressure the physician or pharmacist for early refills, or seek additional sources of supply. Another hallmark of addiction is dishonesty, including dishonesty with the prescribing physician.

In Canada and the United States, legislation prohibits people from acquiring a narcotic prescription without informing the physician of other narcotics that have already been prescribed for them that month. Failure to do so can result in criminal charges. Physicians can record a patient's responses to questions about other prescribed narcotics, and about controlled drugs in general, as a means of discouraging multidoctoring. Several approaches are being developed to help combat multidoctoring through the use of pharmacy information databases. Since the early 1990s, insurers (including state Medicaid programs) have been performing drug utilization review (DUR) surveillance to attempt to identify those involved in multisourcing. In addition, regional and national pharmacy chain stores have developed computer prescription systems to help track prescription use patterns, and they can sometimes identify multisourcing. Several states, beginning with Kentucky in the mid-1990s, have implemented statewide controlled-drug databases, which are available on a password-protected basis to physicians. These databases can provide real-time reports of all scheduled-drug prescriptions filled at pharmacies in the state during the prior 12 months, as well as the number of different prescribers involved. Federal legislation has enabled the NASPER (National All Schedules Prescription Electronic Reporting Act) system to begin to further this initiative on a national level.

Physicians themselves may be involved at various levels in multidoctoring and the diversion of drugs to the street. Some physicians, known as "script doctors," willfully prescribe controlled substances to people seeking them. Others prescribe them as a result of being misled ("duped doctors"), while some are simply uninformed about the prevalence of multidoctoring and the substances involved ("dated doctors"). Educating the public about the risks of prescription medication abuse and increasing the skills of physicians, pharmacists, health-care organizations and state and federal regulators in recognizing patients engaged in multidoctoring will help to decrease the diversion and misuse of prescription drugs.

See also **Prescription Drug Abuse.**

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MUSIC. "Opium? No! Cocaine? No! The Great American Brain Killer Is Dance Music!" Although printed in the Portland *Oregonian* in 1932, that quote neatly encapsulates the fears of mainstream society even today about the link between drugs and music: that outlaw musicians will lead our innocent children Pied Piper-like to their doom with their wild rhythms and coded songs glamorizing the use of drugs.

1930S THROUGH 1960S

Since the 1930s, all the main genres of popular music have been associated with certain drugs, although the nature of that relationship is often multilayered. For example, the use of heroin among the major jazz artists of the 1950s, such as Charlie Parker, Miles Davis, and Chet Baker, was both a product of a desire to set up barriers between the artist and the audience—to be detached and "cool"—and part of the coping mechanism black musicians used to deal with the

daily miseries and humiliations of being black in 1950s America.

In the 1960s, the drugs-music dynamic was very different. Lysergic acid diethylamide (LSD) was an integral part of a zeitgeist looking for an alternative society through the expansion of consciousness. The effects of LSD directly influenced the sound of psychedelic music and the response of the audience. The three-minute dance song was replaced by the 20-minute meandering guitar exposition absorbed earnestly by young people sitting on the floor gently nodding.

ECSTASY AND THE RAVE

Different again was the use of the drug ecstasy in rave culture. For many, all-night dancing requires some form of stimulant drug simply to stay awake; so cocaine and amphetamines were used by '20s flappers, '50s rock 'n rollers, and '70s punks. Ecstasy (chemically related to amphetamine) was simply the latest manifestation of a decades-old phenomenon. The difference lay in the special effect of ecstasy: to engender a sense of empathy in the user toward other people. Because of this effect, it became known as the hug drug. Those who created the scene were attracted by the notion of having a good night out without all the unpleasantness and violence associated with alcohol consumption, although ecstasy itself was not without its dangers.

MUSICIANS AS WANDERERS

One could argue that musicians are simply reflecting back to their audience the common values they all share in any given youth culture. But mention names such as Jimi Hendrix, Janis Joplin, or Kurt Cobain and they are as likely to be remembered by the public for their involvement in the drug scene as for their contribution as professional musicians. So what is it about drugs and musicians?

Musicians have always been located in the outfield of society. In medieval England, the musician wandered rootless from town to town bringing news and gossip to people who would never travel more than five miles from home in their entire lives. The freedom of musicians to roam gave them an aura of mystery and romance. Flash forward to the rock tours of modern times, and you have musicians out on the road for months or even years at a time. That mantle of freedom still hangs from their shoulders, and with it the sense that they can do what they like and move on. This translates itself to the stage where the rock star becomes a Dionysian figure, a blank slate onto which an audience can vicariously map all its desires and wishes and then go back to the office the next day unharmed. Unfortunately, there have been too many rock stars who believed their own mythology. Living the image offstage as well as on has claimed the lives of many musicians through drugs and alcohol.

THE DRIVE TO CREATE

The musician is also an artist and may well exhibit all the anxieties, insecurities, and frailties attending the drive to create. But unlike the writer or the painter, the musician has to operate in one of the toughest, most unforgiving of industries. The music business is a haven for the unscrupulous and downright crooked, where you are only as good as your last record and where all the egos and paranoia of the entertainment business conspire to wreck your ambition and extinguish your creative spark. Moreover, the musician has to be in the public eye, out on stage performing; many musicians are physically ill before a show.

Drug and alcohol abuse can be a form of self-medication to cope with the uncertainties and vicissitudes of the music business, but it can also be linked to another aspect of creativity known by some jazz musicians as the Charlie Parker death wish. This is the belief that because highly gifted musicians such as Parker, Miles Davis, Jimi Hendrix, and John Lennon used drugs, that is what one has to do to be a creative genius. The reality of course, is that these musicians were exceptional in spite of the drugs, not because of them.

However, it does raise the issue of the role of drugs in creativity. There is no question that at a certain level, moderate use of marijuana and alcohol will engender a feeling of relaxation that can facilitate the flow of ideas and also reduce inhibitions. For example improvising musicians may attempt to extend their playing during a live performance, whereas sobriety might have inhibited that stretch. But it can be limited by diminishing returns. One musician told this author that he felt alcohol helped him play the sounds he heard in his head, but it reached a point where he was drinking

so much that his fingers just could not respond fast enough. It is hard to imagine that the iconic sounds of 1960s psychedelia could have been created without the influence of cannabis and LSD, yet heroin and cocaine have ruined untold numbers of recording sessions when not only musicians but also producers and engineers were too stoned or wired up to function.

LIVES OF FAME

In the late 1980s, Charlie Watts said of 25 years in the Rolling Stones, "It's been five years of playing and 20 years of hanging about." Drug and alcohol use can simply be a way to relieve the boredom of hours spent in airport lounges, hotel rooms, and studios. Then musicians have to be in top form for a two-hour show, pack in some leisure time, and sleep on demand to be ready to rush off to the next gig. On a long tour, it is easy to jump onto a chemical carousel of stimulants and sedatives and find it extremely difficult to jump off.

None of this is meant to be an excuse for musicians abusing drugs and alcohol, but simply to offer a brief overview as to the particular circumstances of the life of the professional musician, which can lead to dependency and, sadly, some tragic newspaper headlines. So substance misuse appears inextricably woven into the fabric of the music business, and therefore it is not surprising that musicians want to write about their drug and alcohol experiences as they write about a range of topics that affect their lives. But this has left the business mired in controversy as claims are made that musicians are encouraging the use of drugs among their young audiences and that they have a duty as role models to be more the model citizen than many of them can seem to manage.

DRUGS AND LYRICS

Since the early 1970s, academics have been conducting content analyses of song lyrics to identity reference to drugs and alcohol. These are invariably expressed in the drug slang of the day, which researchers often refer to as "code" as if to suggest a secret language known only to the musician and the audience. This dates to the 1930s, when jazz musicians under the threat of heavy prison sentences would sing about reefer and muggles (marijuana); kicking the gong around (opium smoking), and wacky dust (cocaine). But as drug use spread more widely into the white, middle class student population in the 1960s, the intention of such content analysis was to highlight the supposed risk that young people would be influenced to try drugs through the coded language of their favorite performers.

For some, the fact that a rock band would sing about drugs at all was tantamount to glamorizing drugs, regardless of the nature of the song. A study by Brian Primack, Madeline Dalton, Mary Carroll, Aaron Agarwal, and Michael Fine, published in 2008, made much of the amount of time young people are exposed to music as opposed to health education in schools. And debate continues about whether the Beatles song "Lucy in the Sky with Diamonds" was really about LSD; even the Beatles have made contradictory comments on this point.

In general, songs fall into two categories: decidedly antidrug or neutral. Few songs actually declare that using drugs is exciting and fun—not least because they would never get airplay. The antidrug song can be found in all genres of music. Examples include "Needle of Death" (folk); "Dat Smell" (rock), "Cocaine" (blues), and "White Lines" (hip hop). Alcohol figures most prominently in country music, where much whiskey is consumed to drown out the many sorrows of the ordinary working man.

These songs are focused on the individual experience of the composer, but there have been a plethora of songs from black soul, hip-hop, and rap musicians commenting on the devastation that drugs, especially heroin and crack, have wrought within the black community. Songs about marijuana err more on the positive side, most prominently in reggae, where marijuana (ganja) is regarded by Rastafarians as a religious sacrament in much the same way that wine is used in Catholicism.

AN EFFECT ON TEENS?

The issue remains whether the exposure young people might have to songs about drugs and alcohol actually affects their own decisions about drug or alcohol use. Karl Witty from the U.K.-based National Collaborating Centre for Drug Prevention made an important point in a 2006 paper about celebrities and drug use: "The fundamental problem with existing media research in the context of celebrity influence is however the notion of

causality. Research hints at causal links but fails to provide substantial evidence to endorse such insinuations, thus only providing largely hypothetical evidence."

Finally, there is the question of whether celebrity drug use sets a bad example for young people. Should popular music stars be role models? These musicians fill concert halls around the world, sell a significant number of recordings and much merchandise, and their posters adorn the walls of thousands of bedrooms. So surely they must influence the behavior of young people when they are known to be drug users? Well, there is not a shred of evidence to support what is, admittedly, a commonsense view. In fact when a group of British teenagers were asked by members of Parliament in March 2008 what they thought of such pop stars as Amy Winehouse and Pete Doherty, whose drug use is regularly featured in the British media, they said they simply felt sorry for them. Politicians in particular are wedded to the idea of using celebrities to warn against the dangers of drugs and are quick to condemn those who indulge. But they miss the point entirely. Young people might aspire to become singers or guitarists (or football players or film stars), but they do not aspire to become drug users, nor do they aspire to become role models for others.

The chances of actually becoming successful in the music business are extremely slim; those who make it (often barely out of their teens) can be suddenly catapulted into the public eye and are then expected to become role models. As for drug use among young people, the real decisions about whether to use drugs and alcohol are firmly rooted in their own personal, social, cultural, and economic environment—not in the antics of the rich and remote.

See also **Internet, Impact on Drug and Alcohol Use; Media; Movies.**

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MYTHS ABOUT ADDICTION AND ITS TREATMENT.

The causes of addiction, its nature, the best ways to treat its symptoms, and the possibility of devising a full, permanent cure remain elusive. Why some people experiment with mood-altering substances, and why some of those people go on to become compulsive substance abusers to the detriment of their health, finances, personal relationships, ability to earn a living, and perhaps to their freedom, is not fully understood. Currently there are two general theories on the nature of addiction. Among addiction scientists, medical professionals, and treatment specialists, the most widely accepted theory of the nature of addiction is called the Disease model, which describes addiction as a "chronic relapsing brain disease." This description of addiction maintains that substance use alters the function of the brain in such a way that the addict becomes just as physically disordered, and just as incapable of managing the course of his or her illness, as a diabetic or a sufferer from heart disease, kidney failure, or schizophrenia.

The second theory or set of notions about addiction disorders is often called the Free Will model, which views the individual as an active agent in becoming addicted and in quitting use. This way of conceptualizing addiction emphasizes the fact that substance-dependent people can and do break their habits through their own volition, and that most people either decline to experiment with drugs in the first place or do so casually. Those who prefer this explanation of addiction point out that no amount of behavior change will free a diabetic or a cancer patient from his or her affliction, but that it is possible, though often difficult, for an alcoholic or a heroin addict to stop using alcohol or heroin, and thus be free of the physical symptoms that defined his or her status as an addict (sometimes assisted by drugs such as methadone, which relieve some of the physical discomfort of withdrawal). Once "detoxified," the

Common belief	Disease model response	Free will model response
1. After detoxification, given compliance with treatment and total abstinence from addictive substances, any changes in the pathways of the brain that had been caused by the abused substance disappear, and the brain returns to a more fully healthy state.	As a chronic, relapsing brain disease, substance dependence is an organic state in which neuro-transmitters in the brain have been altered by constant exposure to a psycho-active substance thereby severely limiting the addict's ability to make free choices. The brain usually returns to a better state of health than when the addiction was at its worst, but it takes a very long time to return completely to the health it enjoyed before the substance abuse began. For many addicts, part of the brain damage is permanent.	With the exception of brain damage caused by neuro-toxic substances such as methamphetamine and alcohol, substance dependence in and of itself does not "scar" the brain. Retained memories of drug-induced pleasure may be triggered in the context of mind set and environmental setting and result in the perception of craving, but the addict can resist acting upon it. Substance dependence does have points in common with some diseases associated with behavior, HIV/AIDS, for example, in that something the sufferer did or did not do is usually the source of his or her condition. However, the substance-dependent person can, and often does, make life-changing decisions that free him or her from the condition – not a choice available to a sufferer of AIDS.
2. Everyone has enough free will not to become an addict.	The choice to try an addictive substance for the first time may be voluntary. Surveys have shown that, as perceptions that drug use is dangerous increase in a population, drug use decreases. Yet freedom even in this choice may be weakened by such factors as peer pressure, a biological predisposition to addiction, (alcoholism, for example, tends to run in biological families), or a valid reason for taking it once (for example, as a pain killer prescribed by one's physician).	While some people seem predisposed to enjoy the sensations induced by psycho-active substances and therefore to seek to repeat the experience, others do not and are not inclined to continue using them. Even so, substance-dependent persons are not rendered completely passive by their addiction. No one would deny that it is very difficult to break addiction's grip but it is not impossible and maybe empowering.
3. Many substances are instantly addictive—one experiment will lead inexorably to a full-blown habit.	Addiction is a process. As the person slips from the first use to repeated use to misuse to full-fledged addiction and chemical dependence on the substance, freedom of choice diminishes and usually disappears. The term "disrupted self-control" has been used to describe this process by which the neural structures that underlie decision making are damaged by exposure to psycho-active substances.	Addiction is a process but there are many "exit ramps" along the way. Recovering addicts should not be encouraged to believe that they did not participate in any way in the process.
4. Addiction ends when detoxification removes all of the abused substance from the addict's body, and the pain following detoxification (the withdrawal syndrome) is gone.	Changes in the pathways of the brain, which had been caused by the abused substance, persist long after the last particle of the abused substance has left the body. The underlying addictive disorder (the cause, or set of causes, which made the person liable to become addicted in the first place) remain.	While the impact of the addiction experience on the psyche (and, less romantically, the brain) is profound, so is the impact of other experiences, both positive and negative. How long does it take to repair a "broken heart" after a love affair or the death of a loved one? Surely a long time, but the suffering lover will go on to love again, and the addict can strive to build, and succeed in building, a normal life.
5. A single, simple course of treatment ought to produce a permanent total cure in an addict. When a patient relapses (returns to addiction) after detoxification, then the detoxification of this patient must have failed as a treatment.	As a chronic disorder, addiction needs a lifelong treatment, like diabetes, asthma, arthritis, and high blood pressure, not just a one-time detoxification. One does not expect a single injection of insulin to cure a diabetic, or any single administration of medicine to relieve a patient forever of arthritis, asthma, or high blood pressure. Each treatment is successful if it improves the condition at the time; each needs to be repeated, often throughout the rest of the patient's life.	12-Step Programs such as Alcoholics Anonymous provide successful long-term support for many recovering addicts. Others find the strength necessary to minimize relapse in religion or in stable relationships with significant others. Still others may cycle in and out of treatment programs until they find their personal route to long-term sobriety. This may take as long as a decade but rarely is it longer than that. Meanwhile, while a substance-dependent person is in treatment, harm to self, family, friends, and society is reduced.
6. Once an addict is detoxified, as long as he or she does not take the abused substance (or a different abused substance) again, any medical, social, and occupational difficulties that had been associated with the addiction disappear.	Medical, social, and occupational consequences may last long after an addict has stopped taking any abused substance. Getting sober (detoxification) and remaining sober (compliance with the prescribed treatment) do not automatically repair the damage of a life of addiction. Active alcoholism, for example, may be gone, perhaps forever, but the destruction it may have caused often lasts indefinitely.	The task of rebuilding a responsible life after substance dependence is under control is difficult in the extreme, but it is not impossible. Hope for new relationships and a productive life for the ex-addict, as well as recognition that one is or has been substance-dependent, are essential to recovery.
7. Since most persons treated for addiction relapse sooner or later, treatment is by definition unsuccessful, and it makes no sense to try it.	Treatment is not unsuccessful because further treatments are needed. With addiction, as with diabetes, we must see treatment as an ongoing process, successful if at the time it reduces the severity of the disorder. It unfortunately does	Statistics on treatment success and failure are necessarily drawn from populations in treatment. A large percentage of substance dependent persons break their habits without treatment. This is particularly obvious in the case of tobacco but it is

[CONTINUED]

Table 1. Common beliefs about addiction and responses associated with general concepts about its nature. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Common belief	Disease model response	Free will model response
	not have a permanent fix, like setting a broken bone or surgically removing all of a cancer. The goal is improvement, not cure.	also true for other substances.
8. There are no degrees of addiction. It is an all-or-none condition. A person is either a non-addict and never takes the tiniest amount of an abused substance or is a hopeless addict whose life centers on enjoying maximum amounts of the abused substance (or substances) all day every day for life.	**Agreement between the two Responses** At one extreme, there is an occasional addict who is satisfied with minimal intake and who functions well at home and on the job. At the other extreme is the addict who regularly takes such huge volumes of the abused substance as to lose consciousness. There is, indeed, a formal system for measuring the severity of a patient's addiction and the success of treatment at any given moment. It is called ASI (for ADDICTION SEVERITY INDEX). It considers such factors as whether the patient's substance abuse is decreasing, whether the patient is functioning better socially and enjoying better general health (rarely a complete return to the state before the first use of the abused substance), and to what degree, if any, the patient presents a danger to public health and safety (treatment of an alcoholic who continues to drink but has stopped driving after drinking as a result of psychotherapy would be a partial success).	
9. Most substance-dependent persons engage in criminal activities, either to finance their habits or because their judgment is impaired by alcohol or other drugs.	**Agreement between the two Responses** The drug/crime relationship is difficult to quantify because: • Most crimes result from a variety of factors (personal, situational, cultural, economic); even when drugs are a cause, they are likely to be only one factor among many. • What is meant by "drug-related" varies from study to study; some studies interpret the mere presence of drugs as having causal relevance whereas other studies interpret the relationship more narrowly. • Reports by offenders about their drug use may exaggerate or minimize the relevance of drugs; drug-use measures, such as urinalysis that identifies only very recent drug use, are limited. The evidence indicates that drug users are more likely than nonusers to commit crimes, that arrestees frequently were under the influence of a drug at the time they committed their offense, and that drugs generate violence. Assessing the nature and extent of the influence of drugs on crime requires that reliable information about the offense and the offender be available and that definitions be consistent. In the face of problematic evidence, it is impossible to say quantitatively how much drugs influence the occurrence of crime http://www.whitehousedrugpolicy.gov/publications/factsht/crime/index.html.	
10. If treatment were possible, it would cost millions of dollars to treat a single patient. Treatment would cost more than putting a young person in prison for life. In terms of dollar value, treatment would cost even more than a single addict would be apt to steal in a lifetime.	One study in California showed that the benefits of treatment outweighed the cost of treatment at least four-to-one and as high as twelve-to-one, depending on the type of substance abused and the type of treatment employed. It is non-treatment that costs the United States billions of dollars a year.	Drug court "treatment" of addicts who are also criminal offenders is cost-effective and an excellent behavioral therapy that seeks to hold users accountable. Methadone treatment is inexpensive and reduces risk of HIV, incarceration, homelessness, and emergency room visits.
11. Even if methadone keeps an addict away from heroin, the methadone itself will leave the patient drugged and dangerous, so the patient might as well have stayed on heroin.	Methadone simply does not cause a drugged state, or even the appearances of a drugged state.	Methadone will not change the character of the recipient. A normal dose will mitigate withdrawal and suppress irritability thus reducing the possible harm to individuals and society. Criminal behavior will occur at a lower rate.
12. Even if methadone keeps an addict away from heroin and even if the methadone does not seem to leave the patient drugged and dopey, the patient could function successfully only at undemanding jobs such as raking leaves or checking out books in a library. Even this relatively fortunate patient would be, in effect, in a dangerous position in a job requiring quick reflexes or motor skills, a job such as driving a subway train or operating a forklift.	**Agreement between the two Responses** Patients on methadone can safely drive trains and run forklifts. Some people on methadone cannot do so. The difference between these two groups is not caused by the methadone but by pre-existing factors such as lack of education, physical or psychological problems. Methadone will not create or increase a danger even for these high-risk jobs, but neither will methadone remove a risk caused by a previously existing condition.	

Table 1 (continued). Common beliefs about addiction and responses associated with general concepts about its nature.
ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

addict can choose to begin the process of overcoming the social and personal consequences of a life of substance abuse.

The disease analogy does help to make addiction more comprehensible and less threatening to the general public. Many conditions that were once considered moral failings—sickle-cell anemia and other anemias, for example—are now understood as having a biological or neurological basis (Wailoo, 1999). Similarly, conditions that were considered the result of "bad habits" or effects of a pattern of immoral behaviors—including associating with the "wrong" kinds of people (e.g., polio or HIV/AIDs)—have typically taken a longer time to be recognized as diseases. The idea that dominant notions about disease transmission shape responses to its containment has been a major theme in the history of medicine. Polio so contradicted epidemiological models of disease transmission that lack of cleanliness was not recognized as an exacerbating factor until well into the twentieth century (Rogers, 1992). Addiction remains one of the last bastions of the belief that moral weakness or failures of will are responsible for the disease.

Nevertheless, advocates of the Free Will model would argue that addiction is, in the end, a problem of behavior. In this conception, relieving the addict of responsibility for his or her actions creates an unhealthy dependency on treatment providers and does not help the addict undertake the difficult but essential tasks of recognizing the consequences of substance use and rebuilding ties to mainstream society—of "getting a life," as the saying goes. Advocates of this point of view often maintain that efforts to mitigate the shame that a substance abuser may feel, far from encouraging him or her to seek treatment, exempt the addict from the social norms that human communities have developed to control "antisocial" behavior among their members.

Table 1 lists common beliefs about addiction, each followed by the responses associated with these two general concepts about its nature. Note that advocates of the two models are in agreement on some of their responses.

See also **Addiction: Concepts and Definitions.**

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N

NALOXONE. Naloxone is an opioid antogonist (i.e., a blocker of morphine-like agents) commonly used to reverse the actions of drugs such as morphine. In the early twenty-first century, it was the treatment of choice for reversing the life-threatening effects of opioid overdose. Structurally, naloxone is very closely related to oxymorphone, both compounds being derivatives of the opium alkaloid thebaine. Indeed, the structural differences between oxymorphone and naloxone are minimal; they are restricted to a simple substitution on the nitrogen atom. Oxymorphone has a methyl group whereas naloxone has an allyl substitution. This small substitution changes the pharmacology of the compound dramatically. Whereas oxymorphone is a potent analgesic with actions very similar to morphine, naloxone has no analgesic actions by itself and instead has the ability to antagonize, or reverse, virtually all the effects of morphine-like drugs. This ability to reverse opiate actions has proven valuable clinically. However, giving naloxone to opiate addicts will immediately precipitate withdrawal symptoms.

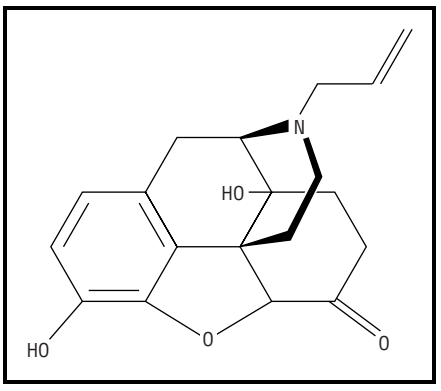

Figure 1. Chemical structure of naloxone. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Naloxone is rapidly metabolized in the liver to inactive compounds, resulting in a relatively brief duration of action. When naloxone is used clinically to reverse the actions of morphine and other opiates, care must be taken to ensure that the drug being reversed does not last longer than the naloxone. Should that happen, a patient may be revived by naloxone only to relapse back into a coma or even die from the side effects of the initial opioid agonist. Despite its effectiveness following injection, naloxone is not very active when given orally; this, together with its short duration of action, prevents its widespread use as a treatment for opioid addiction.

See also **Naltrexone; Opioid Complications and Withdrawal; Treatment, Pharmacological Approaches to: Naltrexone.**

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NALTREXONE. Naltrexone is an opioid antagonist, which reverses or prevents the actions of morphinelike drugs. Its structure is very similar to that of another antagonist, naloxone, and to the potent analgesic (painkiller) oxymorphone.

Replacing the N-methyl group in these two drugs with a methylcyclopropyl group generates naltrexone, whereas substituting an allyl group produces naloxone. The replacement of the N-methyl group of oxymorphone dramatically alters the pharmacology of naloxone and naltrexone.

Naltrexone has no analgesic actions by itself. It has the ability to antagonize, or reverse, virtually all the effects of morphinelike drugs. When given regularly, it can prevent the actions of agents such as heroin, leading some to examine its potential in treating drug abuse. However, its use is limited, and it does not compare to alternative maintenance therapies with methadone or buprenorphine. Like naloxone, naltrexone will precipitate withdrawal in physically dependent people. Naltrexone is rapidly metabolized in the liver, but one of its metabolites is 6-naltrexol, which retains some activity and has a longer duration of action.

Clinically, the use of naltrexone remains limited. It has been used to treat opiate addiction by preventing the actions of heroin, and for the induction of rapid opioid detoxification. It has been approved by the U.S. Food and Drug Administration for the treatment of alcohol dependence following detoxification to reduce the likelihood of relapse. Most recently, a long-acting intramuscular formulation of naltrexone that can be given monthly has been approved and is available in the United States.

See also **Treatment: An Overview of Alcohol Abuse/Dependence; Treatment, Pharmacological Approaches to: An Overview; Treatment, Pharmacological Approaches to: Naltrexone.**

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NARCOTIC. The term *narcotic* derives from the Greek *narkōtikos*, meaning benumbing. It was originally used (since the fourteenth century) to refer to drugs that produced a stupor associated with pain relief (analgesia)—primarily opium and its derivatives, the morphine-like strong analgesics, or the opium-like compounds (opioids). These drugs, in moderate doses, dull the senses, relieve pain, and induce profound sleep; but in large doses cause stupor coma, or convulsions.

During the nineteenth century, the term *narcotic* was widely used to include a number of agents that produced sleep. Toward the end of the nineteenth century, the term came to imply drugs that could lead to addiction, and so by the turn of the twentieth century, "narcotic" came to describe drugs as diverse as opioids and cocaine. During the twentieth century, the term became widely used in a legal context to refer to psychoactive drugs and drugs of abuse—those subject to restriction—as *addictive narcotics*, whether in fact the agents were physiologically addictive and narcotic or not. This imprecise usage has left the term nebulous, although it is still used extensively in the media and by the general population. The term is no longer used in scientific discourse to categorize drugs.

See also **Drug Types; Opiates/Opioids; World Health Organization Expert Committee on Drug Dependence.**

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NARCOTIC ADDICT REHABILITATION ACT (NARA). Public Law 89-793, the Narcotic Addict Rehabilitation Act (NARA), was passed by Congress in 1966. This legislation

was designed to allow the use of the federal courts and criminal justice system to compel drug addicts to participate in treatment. Several developments provided the context for this legislation. In the early 1960s, the problem of narcotic drug use and addiction were perceived to be increasing. There was also a perception that treatment was not particularly effective and that the relapse rate was high. In response, California, in 1961, and New York, in 1962, passed legislation permitting the civil commitment of narcotic addicts; that is, they could be compelled to accept treatment even if they had committed no crime but could be shown to be using illicit narcotic drugs. In both of these states the legislatures also provided substantial funds to establish residential facilities where addicts could be treated initially as well as aftercare programs to provide supervision following their release from the residential facilities. Several other states, including Illinois, passed similar civil commitment legislation, but only New York and California launched massive programs to implement compulsory treatment and civil commitment.

In January 1963, the Presidential Advisory Commission on Narcotic and Drug Abuse appointed by President John F. Kennedy made a number of recommendations, including the enactment of a federal civil commitment statute that could provide an alternative to prison for confirmed narcotic or marijuana abusers convicted of federal crimes. The advisory commission also recommended increased assistance to states and municipalities to develop and strengthen their own treatment programs.

As passed by Congress, NARA had four titles, or main parts: Title I provided that eligible addicts charged with a federal offense could choose civil commitment or treatment instead of prosecution. After being examined by clinicians at a treatment center, an addict, if found suitable, could be committed to the custody of the surgeon general for thirty-six months of institutional treatment and aftercare. Title II provided for civil commitment after conviction. Title III stated that even if no federal crime had been committed, an addict or a related individual could petition the U.S. attorney in the district of residence and, if local facilities were unavailable, the U.S. District Court could commit the person to the custody of the surgeon general for treatment. Title IV provided for funding to states and localities to establish or expand treatment for addicts.

Treatment under NARA began to be provided in 1967. The two U.S. Public Health Service Hospitals—in Lexington, Kentucky, and Fort Worth, Texas—which had been treating both addicted federal prisoners and voluntary patients, were redesignated "Clinical Research Centers" and became the sites for the institutional phase of treatment for addicts committed to the Surgeon General under NARA. Aftercare was provided by local programs supported by contracts with the NARA program administered by the Division of Narcotics within the National Institute of Mental Health (NIMH).

From 1967 through 1973, the two clinical centers admitted more than 10,000 NARA patients: 5 percent under Title I, 2 percent under Title II, and 93 percent under Title III. Women made up 15 percent of admissions. Race and ethnicity were noted for admissions between 1970 and 1973, during which time the designations and distribution were as follows: Anglo, 43 percent; black, 47 percent; Puerto Rican, 1 percent; Mexican American, 9 percent.

Many of the patients referred were found "not suitable for treatment" (38% at Fort Worth and 51% at Lexington), a designation that generally meant they were too disruptive or antagonistic. Some of this unsuitability was deliberate. Many of those under Title III, while not being charged with a federal crime, were under court pressure because of state or local crimes; as part of plea bargaining with local courts, they agreed to accept commitment under NARA Title III. They quickly learned that the centers would not require them to stay in residence, nor would NARA officials compel them to stay in aftercare. Once released from the centers as "not suitable," they would find ways to convey to the local courts how motivated for treatment they still were and how puzzled they were not to be offered treatment.

The general approach to treatment during the residential phase was based on therapeutic community principles, which delegate many responsibilities to former addicts and to patients participating in the program. The average duration of the residential phase of treatment was intended to be about six months, but of those admitted for

examination, only about 35 percent were discharged to aftercare as having completed the residential phase. A number of studies have been conducted on the effectiveness of the NARA program, including aftercare. One study found that only 38 percent of the 35 percent that completed the residential phase remained in aftercare for the full six months after discharge from residential treatment. Reasons for attrition included death, disappearance, recommitment, conviction, and incarceration. One study by Gold and Chatham in 1971 found that 46 percent of addicts in aftercare had used an illegal drug during the month preceding the interview; about 50 percent were working. Another study found that 87 percent had used narcotics during the first six months after the residential phase; 65 percent had become readdicted.

While this rate of readdiction did not seem as bleak as that seen after the discharge of the early cohorts from Lexington, it was not seen as particularly successful, given the high cost of the six-month residential phase and the high attrition rates. Because of the attrition, the readdiction rate, while not inevitable, was occurring among only the better candidates. Another study by Mandell and Amsel (1973) compared the outcome of those treated compared to those found "not suitable" for treatment. The difference in outcome between the two groups was not significant.

While the legal authority for federal civil commitment remained in effect through the early twenty-first, the actual application of NARA fell into disuse in the mid-1970s as more federal prisons developed programs for Title II offenders and as more communities developed their own treatment programs. The use of treatment under civil commitment also declined because the involvement of courts and expensive legal procedures made it far more expensive than voluntary treatment. In 1971, the Fort Worth facility was closed and turned over to the Bureau of Prisons. The Lexington facility experienced the same fate in 1974.

See also **Civil Commitment; Coerced Treatment for Substance Offenders; New York State Civil Commitment Program.**

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NARCOTICS ANONYMOUS (NA).

Narcotics Anonymous (NA) was started in 1953 by Jimmy Kinnon and others who had been regularly attending Alcoholics Anonymous (AA) meetings in southern California. NA broadened the AA program of recovery from alcoholism to recovery from the entire range of psychoactive substances. Using the AA Twelve Steps and Twelve Traditions, Step One was altered to read: "We admitted that we were powerless over our addiction, that our lives had become unmanageable." The first NA World Conference was held in 1971, despite the fact that NA was largely confined to California, with small groups in other major U.S. cities. The late 1970s witnessed sudden rapid growth in NA so that by 1980 an estimated 20,000 people were attending regularly. A World Service Office was opened in 1977 and the first NA World Literature Conference was held in 1979. NA continued to grow steadily around the world so that by 2007 there were over 25,065 groups holding over 43,900 weekly meetings in 127 countries. NA is the second-largest (after AA) twelve-step organization in existence.

THE NA PROGRAM AND HOW IT WORKS

NA is a twelve-step program of recovery from drug addiction, modeled on AA. It is a nonprofit

fellowship of women and men for whom drugs became a major problem. The only requirement for membership is a desire to stop using substances. Membership in NA is free; group expenses are covered by members' voluntary contributions.

Like AA, NA provides meetings in the community and institutions (hospitals, prisons) where members share their experience, strength, and hope. The NA program of recovery is based on the philosophy that addiction is a disease for which there is no cure. Recovery can and will take place if addicted individuals remain abstinent from substances and apply themselves to the program, including frequent and regular attendance at meetings, involvement with a home group (members who attend the same meeting on a regular basis to establish a recovery network and reliable routine), and regular commitment of service to that group (cleaning up, making coffee, etc.), the selection of an experienced NA member to be a sponsor on whom the member may call at any time for advice and guidance through the twelve steps, development of a relationship with a Higher Power based on a personal understanding of what that is, and a gradual but necessary understanding of the twelve steps of recovery. Service may involve taking a more formalized position at the group level, such as treasurer or secretary, or at NA area, regional, and world levels.

There are two basic kinds of meetings: open (anyone is welcome) and closed (limited to addicted individuals). Some meetings are common needs meetings, supporting a particular group based on gender, sexual identity, age, language, and so on (but any addicted person is welcome at any NA meeting). Meeting formats vary, but they often include reading NA literature and open voluntary sharing by people in attendance. Many NA members identify themselves in meetings by their first name only. This spirit of anonymity is based on placing "principles before personalities"; that is, no individual is superior to any other and recovery is not possible without the fellowship or its spiritual principles.

NA has several book-length pieces of fellowship-approved literature. *Narcotics Anonymous: Basic Text* is divided into two books: Book One discusses the basics of the NA program and the Twelve Steps and Traditions, and Book Two presents many personal stories. *It Works: How and Why* offers detailed discussion of the 12 Steps and Traditions. *The Step Working Guides* is a workbook with questions on each step. *Just for Today* is a book of daily meditations with quotations from other NA literature.

RESEARCH ON NA

NA is an important part of addiction treatment systems worldwide. Of the available empirical research on twelve step groups, most has been conducted on AA in the United States, with NA being the next most commonly studied organization. Research on people in substance abuse treatment has found that NA attendance after treatment is associated with less drug use up to five years later (Christo & Franey, 1995; Gossop, Stewart, & Marsden, 2007; Weiss et al., 2005). Weekly or more regular NA attendance is associated with favorable substance use outcomes; less than weekly attendance is no more effective than non-attendance (Best et al., 2001; Fiorentine & Hillhouse, 2000; Gossop et al., 2007). Regular NA attendance is more likely among people with more severe histories of drug use (Brown et al., 2001). In addition, a longer duration of NA attendance has been shown to facilitate both abstinence and long-term improvements in the psychological health (less anxiety; more self-esteem and self-efficacy) and social functioning of its members (Christo & Sutton, 1994; Humphreys et al., 2004; Toumbourou et al., 2002). Furthermore, NA members who engage in other group activities in addition to attending meetings, such as reading program literature, sponsoring new members, applying the twelve steps to daily life, are more likely to abstain from substances than are individuals who do not engage in these activities (Crape et al., 2002; Humphreys et al., 2004). These findings suggest that NA provides a useful supplement to addiction treatment, and regular contact with NA helps to maintain the benefits accrued initially from drug treatment programs (Vederhus & Kristensen, 2006).

See also **Addiction: Concepts and Definitions; Alcoholics Anonymous (AA); Models of Alcoholism and Drug Abuse; Treatment, Behavioral Approaches to: Minnesota Model; Treatment, Behavioral Approaches to: Self-Help and Anonymous Groups.**

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NATIONAL COMMISSION ON MARIHUANA AND DRUG ABUSE.

In response to a substantial increase in drug-use patterns in American society during the 1960s and a swirling controversy about changing the marijuana laws to legalize the substance, in 1970 the U.S. Congress established the National Commission on Marihuana and Drug Abuse. The commission was directed to conduct a two-year study: the first on marijuana and the second on "the causes of drug abuse and their relative significance." The commission was composed of thirteen members, four appointed by the Congress (two each from the Senate and the House) and nine appointed by the president. The chair of the commission was Raymond P. Shafer, former governor of Pennsylvania, and the vice chair was Dana L. Farnsworth, M.D., the director of Student Health Services at Harvard University.

In March 1972, the commission issued its first report, *Marihuana: A Signal of Misunderstanding*, which recommended decriminalization of possession of marijuana for personal use. The commission's final report, *Drug Use in America: Problem in Perspective*, was issued in March 1973. The 500-page report was supplemented by 1,000 pages of appendices. In its report, the commission summarized its findings concerning the patterns of drug use in the United States, psychosocial and institutional influences on drug-using behavior, and the social impact of drug dependence and drug-induced behavior. The commission also proposed a framework for policymaking and made specific recommendations in the areas of legal regulation, prevention, treatment and rehabilitation, and research.

The most enduring impact of the commission's final report probably lies in its efforts to revise the vocabulary of the drug field. The commission insisted that alcohol be recognized as the major "drug" problem in the United States; it recommended that the term "drug abuse" be eschewed in favor of more descriptive terminology concerning drug-using behavior. For example, the commission developed a typology of drug-using behavior (experimental, recreational, situational, intensified, and compulsive use) and emphasized the need for different social responses for different patterns of use. In another important contribution, the commission

fostered the development of information systems for monitoring changes in drug-using behavior in U.S. society, including national surveys of drug-using behavior among high-school students and in the general population.

The commission strongly endorsed the national treatment strategy, codified in the Drug Abuse Office and Treatment Act of 1972, which aimed to create a national network of treatment services and to establish appropriate incentives for people to seek these services voluntarily. In addition, the commission sought to reorient the rule of the criminal law in implementing a policy of discouraging drug use. In the short term, the commission concluded, the criminal sanction should be retained, but should be utilized primarily as leverage for entry into prevention and treatment programs. In regard to government organization, the commission recommended that the law-enforcement and public-health dimensions of national drug-abuse prevention policy be combined into a single agency.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Legal Regulation of Drugs and Alcohol; U.S. Government.**

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NATIONAL COMMISSION ON MARIHUANA AND DRUG ABUSE: RECOMMENDATIONS ON DECRIMINALIZATION.

Before 1960, use of marijuana in the United States was generally confined to drug-using subcultures in the inner cities or in rural areas. Sale and use of the drug were prohibited both by federal law and by the laws of every state. Because marijuana was classified in 1937 as a narcotic drug, along with cocaine and opiates, penalties were severe; simple possession for personal use was a felony in most states. During the 1960s, marijuana use suddenly became prevalent on college campuses for the first time among white middle-class youth of the baby-boom generation. Marijuana use also became associated, as a protest behavior, with dissenters (both adults and youth) against the war in Vietnam, and by the U.S. military serving in Vietnam, especially from 1963 to 1973. As use of the drug increased, so did the number of arrests and so did the surrounding controversy. Questions were raised about the actual effects of marijuana on the health and behavior of those who used it and about the wisdom of prevailing social policy.

In response to swirling controversy, many proposals were introduced in Congress for a commission to undertake an authoritative study of the marijuana issue. Eventually, in the Comprehensive Drug Abuse Prevention and Control Act of 1970 Congress established the National Commission on Marihuana and Drug Abuse to undertake a two-year study—the first year on marijuana and the second year on the causes of drug abuse in general.

The commission had thirteen members—four from Congress (two each from the House and the Senate) and nine appointed by the president. President Richard M. Nixon appointed Raymond P. Shafer, formerly governor of Pennsylvania, as chairman of the commission, and he appointed Dana L. Farnsworth, M.D., director of Student Health Services at Harvard University, to be vice-chairman. The executive director was Michael R. Sonnenreich, formerly the deputy chief counsel of the Bureau of Narcotics and Dangerous Drugs of the Justice Department.

The commission assimilated the available literature on marijuana use and its effects and also sponsored its own research, including a national survey of use patterns and public attitudes, and a study of enforcement of the marijuana laws in six jurisdictions. In March 1972, the commission issued its first report, *Marihuana: A Signal of Misunderstanding.*

PRINCIPAL FINDINGS

The commission estimated that although 24 million Americans had used marijuana at least once,

about 50 percent had simply experimented with the drug out of curiosity and given it up. Among the 50 percent who had continued to use marijuana, most used it only occasionally, once a week or less, for recreational purposes. A small percentage of the more frequent users (about 2% of the total ever-using population—or 4% of the continuing users) used the drug more than once daily. Marijuana use was clearly age-related: about half of the ever-users were 16 to 25 years of age, and 44 percent of those who were currently in college or graduate school had used marijuana at least once.

The commission concluded that there was "little proven danger of physical or psychological harm from the experimental or intermittent use" of marijuana. "The risk of harm," it continued, "lies instead in the heavy, long-term use of the drug, particularly of its more potent preparations." Even this risk was of uncertain dimensions, the commission noted, because the psychological consequences of long-term heavy use were unknown. In light of the fact that 90 percent of marijuana users used the drug only experimentally or intermittently, the commission judged that "its use at the present level does not constitute a major threat to public health." The commission also specifically found that marijuana did not induce physical dependence; did not lead, by virtue of its pharmacology, to use of other drugs; and did not cause criminal behavior.

POLICY RECOMMENDATIONS

The commission's principal policy recommendation was that possession of one ounce or less of marijuana for personal use be "decriminalized." At the same time, the commission rejected outright legalization of the drug and recommended perpetuation of prohibitions against cultivation and distribution for commercial purposes. The commission stipulated that social policy should aim to discourage use of the drug, but it emphasized that the costs of a criminal prohibition against possession far exceeded its benefits in suppressing use.

Although President Nixon disavowed the commission's principal recommendation on marijuana, it won widespread support. In 1973, the National Conference of Commissioners on Uniform State Laws promulgated amendments to the Uniform Controlled Substances Act that codified the commission's recommendation. Some form of decriminalization was endorsed the same year by a variety of national organizations, including the American Bar Association and numerous state and local bar associations, the National Education Association, the Consumers' Union, the National Council of Churches, the American Public Health Association, and the governing board of the American Medical Association.

In 1973, Oregon became the first state to decriminalize possession of small amounts of marijuana. Within the next five years, ten additional states eliminated incarceration as a penalty for simple possession, usually substituting a $100.00 fine. Five of these states made possession a "civil offense"; in others, it remained a criminal offense although the law typically contained a provision for expunction of criminal records after a specified period of time. Decriminalization of marijuana use was endorsed by President Jimmy Carter in 1977.

Political and legislative support for decriminalization began to wane, however, even during the Carter Administration. The more permissive stance on marijuana use implicit in decriminalization efforts led to mounting public resistance. Some of the strongest opposition came from groups of parents who organized to lobby for more focus on prevention efforts. Although these parent groups were generally conservative politically, they gained a receptive ear in the Carter White House. Their arguments against decriminalization were bolstered by findings from the National High School Senior Survey showing that, starting in 1975, daily marijuana use had been increasing progressively among high school students. During the Reagan and Bush administrations the parents' movement and their concerns about marijuana use came to have a major influence on national drug policy. In the early 1990s, possession of the drug remained a criminal offense in most states, as well as under federal law.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Legal Regulation of Drugs and Alcohol; Monitoring the Future; Prevention.**

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NATIONAL COUNCIL ON ALCOHOLISM AND DRUG DEPENDENCE (NCADD). The National Council on Alcoholism and Drug Dependence (NCADD) is the oldest advocacy organization in the United States dedicated to addressing issues of alcohol and drug dependence. It is the country's major public advocate for the prevention and treatment of alcohol and other drug problems, and its explicit mission (reformulated in 2000) is to "fight the stigma and the disease of alcoholism and other drug addictions." Working through hundreds of local affiliate councils, state councils, and its national offices, NCADD sponsors prevention and education programs, information and referral services, scientific and clinical consensus development, public policy advocacy, and other related activities.

NCADD was established in 1944 as the National Committee for Education on Alcoholism. As the organization grew, its name and scope enlarged. It became the National Committee on Alcoholism in 1950, was renamed the National Council on Alcoholism in 1957, and assumed its present name in 1990.

NCADD was the idea of a single individual, Marty Mann; she was its director until her retirement in 1968 and its guiding spirit until her death in 1980. Mrs. Mann was the first woman to recover from alcoholism through the fellowship of Alcoholics Anonymous (AA). During the early years of her recovery, she became increasingly aware that the United States was uninformed about the disease of alcoholism. She concluded that the resulting stigma and prejudice kept alcoholics and their families from receiving the medical, social, and spiritual help they needed to recover. The structure and traditions of AA prevented it from becoming a public-health agency similar to those concerned with promoting prevention, treatment, and research for polio, tuberculosis, cancer, and heart disease. With the support of the Yale Center of Alcohol Studies, the council incorporated and established an office in the New York Academy of Medicine building in New York City. In 1950 it became independent of Yale. Ruth Fox, a psychiatrist who had helped found the council, became its first medical director in 1958. In 1969 she was succeeded by Frank A. Seixas, an internist.

During its early years, council activity consisted mainly of developing literature and presenting lectures to professional and lay groups on the concept of alcoholism as a disease and of organizing local affiliates to pursue this educational process in their own communities. By 1947 a survey of American adults showed that 36 percent believed alcoholism to be a disease, a remarkable increase from 6 percent who held this view in 1943. As interest in alcohol and drug problems expanded, the council developed and then published in 1972 the first set of medical criteria for the diagnosis of alcoholism. In 1976 it sponsored Operation Understanding, in which 52 men and women known for their contributions in the areas of government, medicine, industry, science, journalism, and the arts publicly revealed their histories of recovery from alcoholism.

During the 1980s, NCADD influenced the United States Postal Service to issue the first postal stamp dedicated to raising public awareness about alcoholism (1981). The organization changed its name and broadened its focus to include the disease of drug dependence and used national advocacy efforts to mandate that all bottles containing alcoholic beverages carry warning labels. NCADD lobbied for establishment of a minimum drinking age in America and established the national toll-free HOPE line to provide information and referrals related to alcohol and drug abuse. This was done in conjunction with the national network television screening of *The Betty Ford Story*. As of

2008, the HOPE line receives in excess of 30,000 calls per year.

In the 1990s the American Society of Addiction Medicine and NCADD collaborated on the creation of a comprehensive definition of alcoholism. Published in 1992 in the *Journal of the American Medical Association*, it is still utilized. During the 1990s, NCADD certified and trained affiliates, developed and implemented a family intervention network, and launched a widely acclaimed prevention program aimed at fostering conversations about alcohol use choices between parents and children. Meryl Streep narrated the companion video for this project, titled *What Should I Tell My Children About Drinking?* Updated versions of these materials continue to be in significant demand.

During the first decade of the twenty-first century, NCADD lauded Representative Jim Ranstad and Senator Paul Wellstone for sponsoring legislation aimed at preventing health care insurers from arbitrarily capping addiction treatment coverage. It held a series of Community Forums addressing issues of stigma and discrimination and successfully collaborated with several other advocacy organizations to prevent the mass marketing of a perfume called "Addiction" and to prohibit the NBC-TV from using national network television as a forum for advertising alcoholic beverages.

These and other activities have made NCADD an important force in the national development of service systems and health policy related to alcohol and other drug problems. NCADD helped establish the first industrial alcoholism programs, the first research society devoted to alcoholism, the first public education campaigns to promote the concept of alcoholism and other drug dependence as diseases, the movement to recognize the special needs of women with substance-related problems, and the national effort to understand and prevent fetal alcohol spectrum disorders (FASD) and FAS (Fetal Alcohol Syndrome).

NCADD is also a leader in the U.S. campaign against alcohol-related highway accidents and in promoting appropriate treatment services for substance-dependent pregnant and postpartum women and their children. Through its local affiliates, NCADD provides direct services, including education and prevention, in school and community settings, as well as information, intervention, and referral counseling, local alcohol- and drug-awareness campaigns, and other related activities.

See also **American Society of Addiction Medicine (ASAM); Association for Medical Education and Research in Substance Abuse (AMERSA); Models of Alcoholism and Drug Abuse; Parent Movement, The.**

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SHEILA B. BLUME
REVISED BY PAMELA V. MICHAELS (2009)

NATIONAL FORENSIC LABORATORY INFORMATION SYSTEM (NFLIS). The Office of Diversion Control of the Drug Enforcement Administration (DEA) sponsors the National Forensic Laboratory Information System (NFLIS). NFLIS systematically collects and catalogs the results of drug analyses previously conducted by forensic laboratories at the regional, state, and local levels.

When drugs are seized by law enforcement agencies, whether they are illicit substances or legal prescription drugs (controlled or noncontrolled) being used in a manner other than that for which they were intended, they are catalogued and put through myriad analyses. By so doing, not only are the substances identified—giving important information as new illicit drugs are developed and trafficked—but the logging process affords an important means of tracking the movement of illicit substances into and out of the country, as well as the movement of drugs around the nation. It is also possible to track the movement of legally manufactured drugs into illegal markets.

NFLIS serves as both a storehouse and a clearinghouse for all local and statewide information and is able to track and record trends by regions and states or for the nation as a whole. The system is sufficiently sophisticated to identify new and existing substances by chemical composition and to ascertain quantity, purity, adulteration (cutting with other substances), and mixture with other drugs. The data and reports generated by NFLIS are used to inform drug scheduling efforts and to develop state and federal policy regarding illegal drug use as well as to provide support for drug enforcement operations.

NFLIS was created in 1997 and published its first annual report in 2000. By the end of 2007, NFLIS had become a nationwide, fully operational information management system, processing nearly 90 percent of the nation's more than 1.2 million drug analysis cases, with affiliated laboratories in 42 state systems; 92 local, municipal, or regional labs; and 1 territorial laboratory. In total, 274 labs submit data to NFLIS. Among the other databases sharing information with NFLIS is the DEA's System to Retrieve Information from Drug Evidence II (STRIDE II), which encompasses data from all of the analyses performed at DEA labs around the country. The overall goal of NFLIS is to incorporate the data from every local, regional, and state forensics laboratory in the United States as well as all federal laboratories.

In the first annual report (published in 2000), the ten most commonly seized/analyzed drugs nationwide were: cannabis (39.68%), cocaine (30.65%), methamphetamine (9.84%), heroin (7.54%), noncontrolled nonnarcotic drugs (0.99%), MDMA (0.73%), alprazolam (0.59%), hydrocodone (0.57%), diazepam (0.48%), and oxycodone (0.40%). The percentage of distribution of these drugs varied widely across regions of the country (South, Northeast, Midwest, and West).

By the midyear 2007 report, the most popular drugs had shifted positions a bit: cocaine (40.61%), cannabis/THC (27.99%), methamphetamine (6.39%), heroin (3.96%), hydrocodone (2.75%), alprazolam (2.83%), oxycodone (1.43%), noncontrolled nonnarcotics (1.04%), MDMA (1.45%), and methadone (0.62%).

See also **U.S. Government; U.S. Government Agencies.**

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PAMELA V. MICHAELS

NATIONAL SURVEY ON DRUG USE AND HEALTH (NSDUH).

The National Survey on Drug Use and Health (NSDUH), formerly called the National Household Survey on Drug Abuse, is the primary source of information in the U.S. federal government on the nature and extent of substance use and abuse in the United States. Conducted since 1971, the survey collects data by administering questionnaires to a representative sample of persons aged 12 or older at their places of residence. Data from the survey are used extensively by policymakers and researchers to measure the prevalence and correlates of licit and illicit substance use, to identify and monitor trends in substance use, and to analyze differences in substance use patterns by population subgroups.

HISTORY OF THE SURVEY

The survey traces its origin to studies conducted by the National Commission on Marihuana and Drug Abuse. The commission was created in 1970 to develop recommendations for legislation and administrative actions to address increasing public concerns about illicit drug abuse. The commission conducted two national surveys, in 1971 and 1972, to obtain data on the public's beliefs, attitudes, and use of marijuana and other drugs. When the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) was created in 1974, with the National Institute on Drug Abuse (NIDA) as one component, NIDA continued conducting the survey to monitor the incidence and prevalence of drug use in the United States. The survey became known as the National Household Survey on Drug Abuse (NHSDA).

Since 1971, the survey has undergone a variety of changes in its sample design as data priorities have changed. During the 1970s and 1980s, it was a relatively small, periodic survey. Conducted every two or three years, the sample size grew gradually from about 3,000 respondents per survey in the early 1970s to 8,814 in 1988. In the late 1980s, the U.S. cocaine abuse problem became a major concern of the public and of politicians. Congress passed legislation that increased funding for substance abuse data collection and created the White House Office of National Drug Control Policy (ONDCP), which began producing annual national strategies that used NHSDA data extensively in setting goals and tracking the progress of drug abuse policies and programs. With the increase in funds and greater reliance on NHSDA data by policymakers and researchers, annual fielding of the survey began in 1990, and a significant expansion of the sample began in 1991. The basic national sample size throughout the 1990s was about 18,000 respondents per year.

The ADAMHA Reorganization Act of 1992 moved NIDA to the National Institutes of Health and created a new services-focused agency, the Substance Abuse and Mental Health Services Administration (SAMHSA). Under this reorganization, the Office of Applied Studies, SAMSHA, was given the responsibility for managing the NHSDA.

Throughout the survey's history, interest in particular subpopulations led to sample design changes and augmentations. Rural areas were oversampled in 1979 and 1994, and the survey oversampled blacks and Hispanics from 1985 through 1998. Supplemental samples of six metropolitan areas were included from 1990 through 1993, and supplemental samples in California and Arizona were added in 1997 and 1998.

Changes in the data collection methodology prior to 1999 were infrequent and relatively minor.

The survey used the same basic methodology from 1971 through 1998: a confidential, anonymous, face-to-face interview conducted in households and employing self-administration of sensitive substance use items. However, some small but important changes were made in the survey procedures that affected survey estimates of substance use prevalence. In 1982, questions on nonmedical use of psychotherapeutic drugs were converted from interviewer-administered to self-administered. Similarly, tobacco questions were shifted to self-administration in 1994. Machine editing procedures were incorporated into the NHSDA data processing for the first time in 1988. In 1994, following extensive research, the NHSDA questionnaire and editing procedures were modified to provide more reliable substance use prevalence estimates.

Methodological research demonstrated the benefits of audio-computer-assisted self-interviewing (ACASI) in collecting data on sensitive behaviors such as substance use in household surveys. Studies indicate that respondents are more willing to report sensitive behaviors with ACASI than with other modes of data collection. Based on this research, SAMHSA decided in 1995 to initiate development and testing of a computer-assisted interview (CAI), including ACASI, in the NHSDA.

At the same time that the new NHSDA CAI was being developed, a long-standing interest in state-level substance use prevalence data was culminating in legislation that resulted in the redesign of the NHSDA sample. With the passage in 1996 of voter initiatives legalizing marijuana use for medical purposes in California and Arizona, and the substantial role of federal block grant funds given to states for substance abuse prevention and treatment, Congress and the Clinton administration concluded it would be useful to have state-level estimates.

Thus, in 1999, a major redesign of the NHSDA was implemented involving both the sample design and the data collection method of the survey. The national design was changed to a much larger, state-based design with 67,500 respondents per year. The data collection method was changed from a paper-and-pencil interview (PAPI) method to CAI, primarily to improve the quality of NHSDA estimates. Then in 2002, in order to improve response rates and more accurately reflect the focus of the survey, the name of the survey was changed to the National Survey on Drug Use and Health, and a remuneration of $30 for all survey respondents was initiated. These two changes, along with enhanced data collection quality control procedures introduced around the same time, affected survey respondents' reporting of substance use, causing a discontinuity in trend measurement between 2001 and 2002.

DESIGN OF NSDUH

Starting in 2002 and expected in 2008 to continue through 2009, the NSDUH was to maintain a consistent survey design, which facilitated trend comparisons and pooling of multiple years of data for in-depth analysis. Details of the design during this period are given below.

Target Population. The respondent universe is the civilian, noninstitutionalized population aged 12 years or older residing within the United States and the District of Columbia. Persons excluded from the universe include active-duty military personnel, persons with no fixed household address (e.g., homeless and/or transient persons not in shelters), and residents of institutional group quarters, such as jails and hospitals.

Sample Design. Eight states (California, Florida, Illinois, Michigan, New York, Ohio, Pennsylvania, and Texas) were designated as large sample states with samples of about 3,600 respondents. For the remaining 42 states and the District of Columbia, samples of about 900 persons were selected. Within each state, samples were equally allocated to three age groups: 12 to 17, 18 to 25, and 26 and older. States were first stratified into a total of 900 state sampling regions (SSR), with 48 regions in each large sample state and 12 regions in each small sample state. These regions were contiguous geographic areas designed to yield the same number of interviews on average (about 75 per year). Within sampled census tracts, adjacent census blocks were combined to form the second-stage sampling units or area segments. One segment was selected within each sampled census tract with probability proportional to population.

Each year, eight sample segments per SSR are fielded. These sampled segments are allocated equally into four separate samples, one for each

Drug	2002	2003	2004	2005	2006
Illicit drugs[1]	108,255[b]	110,205	110,057	112,085	111,774
Marijuana and Hashish	94,946[a]	96,611	96,772	97,545	97,825
Cocaine	33,910	34,891	34,153	33,673	35,298
Crack	8,402	7,949	7,840	7,928	8,554
Heroin	3,668	3,744	3,145[a]	3,534	3,785
Hallucinogens	34,314	34,363	34,333	33,728	35,281
LSD	24,516	24,424	23,398	22,433	23,346
PCP	7,418	7,107	6,762	6,603	6,618
Ecstasy	10,150[b]	10,904[b]	11,130[a]	11,495	12,262
Inhalants	22,870	22,995	22,798	22,745	22,879
Nonmedical Use of Psychotherapeutics[2]	46,558[b]	47,882[a]	48,013	48,709	49,842
Pain Relievers	29,611[b]	31,207[b]	31,768[a]	32,692	33,472
OxyContin®	1,924[b]	2,832[b]	3,072[b]	3,481[b]	4,098
Tranquilizers	19,267[b]	20,220	19,852[a]	21,041	21,303
Stimulants	21,072	20,798	19,982	19,080	20,118
Sedatives	9,960[a]	9,510	9,891[a]	8,982	8,822

*Low precision; no estimate reported.
[a]Difference between estimate and 2006 estimate is statistically significant at the 0.05 level.
[b]Difference between estimate and 2006 estimate is statistically significant at the 0.01 level.
[1]Illicit Drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically. Illicit Drugs Other Than Marijuana include cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically.
[2]Nonmedical use of prescription-type psychotherapeutics includes the nonmedical use of pain relievers, tranquilzers, stimulants, or sedatives and does not include over-the-counter drugs.

SOURCE: SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 2002, 2003, 2004, 2005, and 2006.

Table 1. Types of illicit drug use in lifetime among persons aged 12 or older: Numbers in thousands, 2002–2006. (Source: SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 2002, 2003, 2004, 2005 and 2006.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

three-month period (calendar quarter) during the year, so that the survey is essentially continuous in the field. In each of these area segments, a listing of all addresses is made, from which a sample of about 180,000 addresses is selected. Of the selected addresses, about 150,000 are determined to be eligible sample units. About 91 percent of these eligible units (which can be either households or units within group quarters) participate in the survey, completing a short automated screener on household composition. Based on this information, zero, one, or two sample persons are randomly selected to be interviewed in each unit. The weighted response rate for interviewing in 2006 was 74 percent.

Data Collection Methodology. The data collection method used in NSDUH involves in-person interviews with sample persons, incorporating procedures that increase respondents' cooperation and willingness to report honestly about their illicit drug use behavior. Confidentiality is stressed in all written and oral communications with potential respondents. Respondents' names are not collected with the data, and ACASI maximizes privacy and confidentiality.

Interviewers immediately attempt to conduct the NSDUH interview with each selected person in the household. The interviewer requests the selected respondent to identify a private area in the home as the location for the interview away from other household members. The interview takes about an hour. All respondents who complete a full interview receive a $30 cash payment as a token of appreciation for their time.

A key feature of the interview is a core/supplement structure. A core set of questions critical for basic trend measurement of prevalence estimates remains in the survey every year and comprises the first part of the interview. Supplemental questions, or modules, that can be revised, dropped, or added from year to year make up the remainder of the interview. The core consists of initial demographic items (which are interviewer-administered) and self-administered questions pertaining to the use of tobacco, alcohol, marijuana, cocaine, crack cocaine, heroin, hallucinogens, inhalants, pain relievers, tranquilizers, stimulants, and sedatives. Supplemental topics in the remaining self-administered sections include (but are not limited to)

injection drug use, perceived risks of substance use, substance dependence or abuse, arrests, treatment for substance use problems, pregnancy and health care issues, and mental health issues.

Supplemental demographic questions (which are interviewer-administered and follow the ACASI questions) address such topics as immigration, current school enrollment, employment and workplace issues, health insurance coverage, and income. It should be noted that some of the supplemental portions of the interview have remained in the survey, relatively unchanged, every year (e.g., current health insurance coverage, income). Some questionnaire modules have been included in the survey for a single year in response to requests from other agencies such as the Centers for Disease Control (sexual behaviors module in 1996) and the National Highway Traffic Safety Administration (driving behaviors module in 1996).

ANALYSES OF NSDUH DATA

The following section discusses various issues related to the analysis of NSDUH data, including how the results are reported, access to the data files for research, quality of the data, and how NSDUH estimates compare with estimates from other surveys. Finally, a brief summary of some of the most important findings from NSDUH is included.

Reporting the Results. NSDUH results are made available by SAMHSA in a variety of forms. The first release of each year's national results typically occurs about eight months after data collection is completed. At that time, a comprehensive report of the national results is published, along with numerous detailed tabulations and technical information on the survey, and a press conference is held to announce the results. Subsequently, various other analytic reports focusing on specific issues of interest are produced by SAMHSA from the latest survey. Whereas some studies address trends over time, much of the analysis is done by combining multiple years of data, to increase the statistical power of comparisons between groups and the study of correlates. State-level estimates are published annually using a model-based estimation method (Hierarchical Bayes Estimation) that incorporates each state's sample data with external local area predictors and a national regression model. Two years of data are combined for these state estimates. SAMHSA also periodically produces sub-state estimates, based on at least three years of data.

Access to Data Files. Complete analytic data files are used by NSDUH project staff to produce SAMSHA reports and special analyses. These files have not been made available to analysts outside the project because of legal requirements to protect the confidentiality of survey respondents. However, project statisticians often provide special tabulations or analyses when requested, subject to the availability of resources to support this work. Public use data files are made available free of charge to researchers within 12 months of the completion of data collection. These files are created through a process of disclosure limitation that maximizes the utility of the data for various analyses, while eliminating the risk that the identities of respondents could be ascertained by persons accessing the files, which is done using a combination of techniques, including random removal of records, elimination of identifying variables (especially geographic location data), and recoding of some variables. As of the early twenty-first century, SAMHSA had initiated procedures to make the full analytic NSDUH data files available to researchers, following guidelines specified in the Confidential Information Protection and Statistical Efficiency Act of 2002 (CIPSEA).

Strengths and Limitations of the NSDUH. The major strengths of the NSDUH are its size, continuity, and representativeness. The survey has a sample large enough to allow detailed analysis of small subgroups (sociodemographic or geographic) and for rare characteristics. The comprehensive questionnaire provides a rich database for examining multiple factors associated with various substance use behaviors and problems, including substance use initiation, dependence and abuse, and treatment. The methodology employed in NSDUH has been extensively evaluated and found to be effective in eliciting valid data from respondents. Participation rates are excellent, with 91 percent of selected households participating and 74 percent of selected persons participating in 2006. The major limitations are the exclusion of certain high-risk subgroups (homeless not in shelters, incarcerated persons, and those in long-term health care facilities) and the reliance on self-report. NSDUH estimates

for most illicit substances, especially heroin and cocaine, are generally considered to be conservative.

Comparisons with Other Surveys. NSDUH is one of several national and local surveys that assess substance use prevalence. Each survey may have its own purposes, definitions, and design. Nevertheless, policymakers and epidemiologists often compare and contrast the findings from these different data sources, which can sometimes lead to confusion and skepticism when findings differ. Research has established that surveys of substance use and other sensitive topics often produce inconsistent results because of different methods used. For example, reported levels of substance use increased significantly in NSDUH when the incentive payment and name change were introduced in 2002. School-based surveys collecting data in classrooms have consistently reported higher levels of substance use than surveys such as NSDUH that collect data from youths in households. Moreover, household surveys like NSDUH that collect data using self-administration (respondents answer questions privately) tend to obtain higher levels of substance use than surveys in which interviewers record the verbal responses of survey participants. Other factors that can account for differing results across surveys are definitions used, populations covered, and low response rates, which are a particular problem in telephone-based surveys.

FINDINGS FROM NSDUH

Regarding substance use prevalence, the 2006 NSDUH estimated that nearly half of the U.S. adults aged 18 or older (47.5%) had used illicit drugs in their lifetime, and 8.3 percent were current (past month) users. Among youths aged 12 to 17, more than one-fourth (27.6%) had ever used and 9.8 percent used currently. However, there are wide variations in use rates by age, with 3.1 percent of 12-year-olds and 17.1 percent of 17-year-olds using in the past year. Similarly, among adults, the past year rate was 22.2 percent among young adults 18 to 20, but only 6.0 percent among persons age 50 to 54 and below 1 percent for those aged 65 or older. Periodic changes in the survey methodology have limited the ability of NSDUH to track trends, but the survey has documented important trends such as the substantial increases in marijuana and other illicit drug use during the 1960s and 1970s, followed by significant declines during the 1980s. Reaching a low point in 1992, the rate of use among youths had nearly tripled by the end of the decade then declined slightly from 2002 to 2006. Trends among youth reported by NSDUH have been very similar to those seen in other youth surveys, including Monitoring the Future and the Youth Risk Behavior Survey.

Regarding other key findings, the depth of the NSDUH interview and wide population coverage facilitates investigation into many areas of interest to policymakers and researchers. The data have been critical in quantifying substance abuse treatment need, estimating that about 23.6 million Americans needed treatment for a substance use problem in 2006, while only 2.5 million (10.8%) had received specialty treatment. Only 4.5 percent of the 21.1 million persons needing but not receiving treatment actually reported that they perceived a need for treatment. NSDUH data have also been widely used in the study of underage drinking. The survey estimated that in 2006, 28.3 percent of youths aged 12 to 20 were current drinkers and that this rate had been unchanged since at least 2002.

See also **Drug Abuse Warning Network (DAWN); Monitoring the Future; U.S. Government Agencies; U.S. Government Agencies: National Institute on Drug Abuse (NIDA).**

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JOSEPH GFROERER

NEEDLE AND SYRINGE EXCHANGES AND HIV/AIDS.

AIDS (acquired immunodeficiency syndrome) was first observed in homosexual men and injecting drug users (IDUs) in 1981. The discovery of the human immunodeficiency virus (HIV) and the development of a test for the HIV antibody in 1984 and 1985 confirmed that AIDS could be transmitted through the micro-transfusions that occur when IDUs share needles and syringes. HIV antibody testing also indicated that large numbers of IDUs were already infected with HIV—approximately 50 percent in New York City (Des Jarlais & Friedman, 1988) and Edinburgh (Robertson et al., 1986; Skidmore, Robertson, & Savage, 1990) and over 30 percent in Amsterdam (Buning, van Brussel, & van Santen, 1988). Two types of innovative programs, community outreach and syringe exchange, were developed in order to reduce HIV transmission among IDUs.

Outreach programs (Coyle, Needle, & Normand, 1998) use trained health-care workers to provide AIDS education to IDUs in the community. The outreach workers are usually former drug users, although sometimes individuals with good knowledge of the community but without any personal history of drug use are employed, as are active drug users. These outreach programs are effective in educating IDUs about HIV and AIDS and in motivating change in their behaviors (NIH, 1997).

INITIAL SYRINGE-EXCHANGE PROGRAM DEVELOPMENT

The first syringe-exchange program was instituted in Amsterdam in 1984, out of concern about the Hepatitis B virus not HIV infection. A large pharmacy in the city center changed its policy and stopped selling needles and syringes to drug injectors. The local health department then worked with the Amsterdam drug users' union (Junkie Bonden) to establish a program whereby drug users would turn in their used needles and syringes for new ones at no cost. Within a year HIV antibody testing started in Amsterdam, leading to the realization that a substantial percentage of local IDUs were already infected with HIV (Buning, 1991). The syringe-exchange program was then rapidly expanded.

Syringe-exchange programs were subsequently implemented in many locales in the late 1980s. In most industrialized countries, syringe exchange became part of the national AIDS prevention plan. The United States and Sweden were the two notable exceptions, but even in these nations syringe-exchange programs were often implemented at the local level. The first regular syringe-exchange programs commenced in the United States in 1988, and there were approximately 180 such programs as of 2006 (McKnight et al., 2007).

EFFECTIVENESS OF SYRINGE-EXCHANGE PROGRAMS

A large number of studies have evaluated syringe exchange, both in the United States and in other industrialized countries (NIH, 1997; Normand, Vlahov, & Moses, 1995; Committee on the Prevention of HIV Infection, 2006; Des Jarlais et al., 1996; Stimson, 1995; and Wodak & Cooney, 2006). All concluded that syringe-exchange programs are effective in reducing HIV transmission among IDUs, and that they are best implemented as part of a comprehensive HIV prevention program for drug users, including community outreach and drug abuse treatment.

Even the best syringe-exchange programs do not eliminate injection risk behavior (the sharing of needles, syringes, and other drug injection equipment) among IDUs. (There are no HIV prevention programs that eliminate risk behavior in any population at high risk for HIV.) Because of the continuation of some injecting risk behavior, syringe-exchange programs and HIV prevention programs, in general, are best begun when few persons infected with HIV exist within the local population. If syringe-exchange and community outreach programs begin when HIV infection rates are low (an HIV prevalence of 5% or

less), it is possible to prevent HIV epidemics among IDUs (Des Jarlais et al., 1995).

Controlling an HIV epidemic that has already reached a high level of infection (an HIV prevalence of 20% or greater) is considerably more difficult. With large numbers of individuals capable of transmitting HIV and large numbers susceptible to becoming infected, even moderate rates of risk behavior can lead to unacceptably high rates of new infections. There is increasing evidence, however, that syringe-exchange and other HIV prevention programs for IDUs can halt high HIV prevalence epidemics among IDUs (Des Jarlais et al., 2005; Lindenberg et al., 2006).

Although syringe-exchange and community outreach programs generally may be highly effective in reducing HIV transmission among IDUs, not all individual programs have controlled HIV transmission in the local population of IDUs. Vancouver, Canada, experienced an outbreak of HIV transmission among IDUs despite having a syringe-exchange program. Multiple factors contributed to this outbreak, including a change from heroin to cocaine injecting, which requires many more syringes if safe injection is to be practiced, a strict limit (4) on the number of syringes that could be exchanged at each visit, and concentration of the homeless or multiply disadvantaged IDUs in a specific area of the city (Strathdee et al., 1997).

LACK OF UNDESIRABLE CONSEQUENCES

When syringe-exchange programs were first proposed, intense opposition existed in several countries—particularly the United States and Sweden. Fears were expressed that syringe exchanges would lead to increases in illicit drug injection and to greater numbers of syringes discarded in public places. None of these undesirable consequences has occurred. Because so many syringe-exchange programs assist drug users in entering drug abuse treatment, they have probably led to a reduction in the numbers of illicit drug users. And because the existence of a syringe-exchange program gives economic value to a used syringe (it can be exchanged for a new sterile syringe), exchanges have probably led to a net reduction in the number of used syringes discarded in public places (Committee on the Prevention of HIV Infection, 2006).

SYRINGE-EXCHANGE BEST PRACTICE: SECONDARY EXCHANGE

The core idea of syringe exchange is that a drug injector brings used needles and syringes to the exchange and is then given new sterile ones. A very important corollary to this basic concept is that drug users should be able to exchange syringes not only for their own personal use but also for their peers (what is known as *secondary exchange*). Secondary exchange's major benefit is providing syringe exchange to injectors who cannot or do not want to personally attend a program. Given that most programs have limited hours of operation and a limited number of sites, and that many drug users need to protect their confidentiality, secondary exchange is a critical aspect of HIV prevention for IDUs in many communities.

Programs can encourage secondary exchange in several ways. First, there should be no limit on the number of needles and syringes that can be exchanged in a single visit to the program. In many programs, it is not unusual for an individual to exchange hundreds of used needles and syringes in a single visit. Many programs now train selected participants to provide peer-delivered syringe-exchange services, including education and referral services in addition to sterile syringes.

SYRINGE-EXCHANGE BEST PRACTICE: MULTIPLE SERVICES

In addition to the core mission of providing access to sterile needles and syringes in order to reduce HIV transmission, the great majority of syringe-exchange programs provide a variety of other services. These services can be offered either on site at the exchange or through referral. In the United States, the vast majority of syringe-exchange programs (90% or more) provide condoms, alcohol pads for cleaning skin prior to injection, referrals to substance abuse treatment, education on Hepatitis A, B, and C prevention, education on safer injection and vein care, and HIV counseling and testing. Forty to 80 percent provide clothes, food, and hygiene items, HAV and HBV vaccination, and screening for sexually transmitted diseases (McKnight et al., 2007).

Although the continuing importance of reducing HIV transmission among IDUs cannot be overestimated, syringe-exchange programs have evolved into organizations that provide a wide variety of health and social services to a highly vulnerable population.

Given the modest budgets of most syringe-exchange programs, the generally excellent relationships between the programs and their participants, and the high cost of providing services to IDUs through the usual settings such as emergency rooms, the provision of multiple services via syringe-exchange programs is almost certain to be highly cost-effective.

LOW- AND MIDDLE-INCOME COUNTRIES

While syringe exchange may be considered a highly successful health-care innovation in high-income countries, the situation is much more problematic in low- and middle-income nations. According to one recent estimate (Aceijas et al., 2006), there are 13 million IDUs in the world, and over 10 million of them live in low- and middle-income countries. HIV continues to spread rapidly among IDUs in many parts of Eastern Europe and Asia (UNAIDS/WHO, 2007). In general, syringe exchange (and other programs to prevent HIV transmission among IDUs) have been implemented only at the pilot program level in low- and middle-income countries (Sharma, Burrows, & Bluthenthal, 2008).

Scaling up HIV prevention for IDUs in low- and middle-income nations presents a unique public health situation. The technology for controlling HIV transmission is readily available. The challenge is developing the political will and resources to implement programs for a highly stigmatized population.

HARM REDUCTION

The public health crisis of HIV transmission among IDUs and their sexual partners that led to the wide-scale adoption of syringe-exchange programs has also furthered policy development in the drug abuse field. HIV transmission among IDUs is a clear example of when an individual and social harm associated with illicit psychoactive drug use can be greatly reduced without having to solve the underlying very difficult problem of getting people to stop using drugs. As such, syringe exchange epitomizes what has become known as the *harm reduction* approach to the problems of psychoactive drug use (IHRA, 2008).

Harm reduction is based on two fundamental principles. First, drug users are seen as members of the community, having human rights and deserving to be treated with dignity and respect. Second, programs and public policy should be based on empirical evidence of what does and does not work rather than on symbolic value.

Given the nature of the human nervous system, it would not seem possible to create societies that do not include psychoactive drug use. At the same time, advances in scientific research on psychoactive drug use will create new opportunities to address the many problems associated with legal and illicit drug use. Harm reduction offers a perspective within which new scientific knowledge can be incorporated into public health (Des Jarlais, 1995).

See also **Alcohol and AIDS; Complications: Route of Administration; Injecting Drug Users and HIV; Substance Abuse and AIDS.**

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DON C. DES JARLAIS

NETHERLANDS. Drug use in the Netherlands occurs in the context of a specific culture of informal social control and a liberal and nonrestrictive national drug policy that has sustained itself for almost a half century. After the explosive global growth of drug use in the 1960s and 1970s, the Dutch government moved away from traditional prohibition policies and developed a national policy of "harm reduction." Since then, many countries have adopted the innovations in harm reduction developed in the Netherlands. In addition, since the late 1990s, the emphasis of the Dutch harm reduction policy has been modified and more focused on "risk reduction." Health protection and risk reduction among vulnerable populations in the society has become the national policy priority. These vulnerable populations include various categories of youth, ranging from ethnic minority neighborhood youth to homeless and detained youth and schoolchildren and adolescents. New techniques for screening and early intervention to protect health using multidisciplinary teams utilizing genetic and social risk profiles have also become an emerging instrument of national policy.

The harm reduction drug policy of the Netherlands has been built on two main principles—the separation of the markets of so-called soft drugs (e.g., cannabis) and hard drugs (e.g., heroin and cocaine), and the normalization of drug problems. The "separation of markets" principle is based on the idea that drugs can be classified pharmacologically according to their socially acceptable risks, and that drug markets should be controlled on the basis of this classification.

CANNABIS

In the Netherlands, cannabis has been considered a drug of acceptable risk. Tolerating the sale and use of cannabis in "coffee shops" (cafes in which cannabis can be bought and used but that do not serve alcohol) was seen as a way of controlling and normalizing this drug use in society. With the sale of cannabis tolerated in a socially visible and acceptable market (although formally illegal), it was felt that the informal social control of society would be increased. Local authorities could impose standardized regulations and enforcement techniques that could be compared to alcohol and tobacco control.

Dutch jurisprudence, through the "opportunity principle," was used to legitimate this approach, by which the local criminal justice authorities could choose not to enforce a given law if the social harm caused by this action was greater than the crime itself. The latest figures from 2005 show that there are coffee shops in 105 of the 467 cities in the Netherlands, with a total of 729 shops in the country. Most cities of under 50,000 population do not have coffee shops, and the relatively larger cities that do have coffee shops show a rate of 0.55 coffee shops per 10,000 habitants.

The official position on cannabis, however, is showing signs of change in light of the modifications to the original harm reduction policy, which was predicated on a model of informed individual decision making. This policy has been giving way instead to a policy of public health protection. A tendency toward stricter control measures can be observed, and any deviance from the regulations is enforced. The government clearly wants fewer coffee shops in the country, and none are wanted near schools or border crossings (where "drug tourism" creates problems related to all types of drugs). Specifically, under pressure from the government, more and more municipalities have imposed regulations that do not allow a coffee shop to be located within about 250 meters of a school. In order to reduce the problem of drug tourists, discussions are under way concerning how far a coffee shop can be from a national border. Coffee shops have also been experimentally placed outside city centers. Hallucinogenic mushrooms, which are sold in "smart shops" (a kind of specialty shop that sells fresh mushrooms, cognitive enhancers, and high energy preparations but does not allow the use of these substances on the premises), have also been gaining popularity with drug tourists. Because of this and other alleged problems, the government has been moving to close these smart shops and place hallucinogenic mushrooms under the Opium Law, the criminal statute for drugs in the Netherlands.

Cannabis trafficking has been, and remains, clearly illegal in the Netherlands. The so-called AHOJ-G policy for marketing cannabis has been sustained and expanded. This policy requires the coffee shops to: limit advertising (A); not sell hard drugs (cocaine or heroin) on the premises (H); have no social nuisance (O, or "overlast, meaning offenses to the public order"); have no youths under 18 years of age on the premises (J); sell only small amounts (G), meaning 5 grams per transaction, with a maximum of 500 grams in stock. Additional local regulations are also in force, and serving and consuming alcohol is not allowed in coffee shops. There are also regulations regarding the locations where coffee shops can do business. Despite the existence of this extensive coffee shop system, an illegal cannabis market also exists, consisting of fixed sales points such as house dealers, under-the-counter sales in pubs and cafes, and mobile sales through cell phones and home delivery services. Law enforcement efforts are vigorous in suppressing these nontolerated markets and keeping cannabis distribution within the formal social control of the coffee shop system.

IMPACT OF DUTCH POLICIES ON INTERNATIONAL RELATIONS AND CONTROL

The drug policies of the Netherlands have been continuously criticized because of the perception that the country has become an international center of drug use and drug trafficking. This perception is changing, however, in light of new developments in law enforcement and the criminal justice system. Since the coffee shops were established, they have been a continuous source of tension between the Netherlands and its neighbors. The Schengen Accord, an agreement on border control among 9 European nations, went into effect in 1995 and made an official distinction between "inner" and "outer" borders, with the trafficking in drugs and the existence of coffee shops forbidden along these borders.

In the past, most of the pressure on the Netherlands was asserted at the national level from the European Union, and the Dutch government issued a "Cannabis Letter" in 2004 that acknowledged that the coffee shops were damaging the international relationships of the Netherlands. Earlier, Germany had argued forcibly that the Dutch coffee shops, as well as the "low threshold" methadone programs, undermined their prevention and treatment policies for reducing youth drug use. Along this same line, in 1999 the French president had threatened to close France's inner border in response to drug tourism, though his remarks had

the unanticipated effect of increasing the number of young French drug tourists. These kind of international events surrounding the interpretation of the Schengen Accord resulted in a decision within the European Union to encourage the member states to articulate a policy on drug tourism as part of their actions against drug trafficking.

The international tensions still persist in the first decade of the twenty-first century, but they seem to be expressed more and more at the local level in the border areas. For example, it is estimated that each week 22,000 Belgian and French drug tourists buy cannabis from coffee shops in Bergen op Zoom and Roosendaal, two Dutch cities close to the Belgian border. Some Dutch communities have implemented a zero tolerance policy on coffee shops while others have initiated special restrictions. While the local Dutch communities have worked hard to develop an effective policy to restrict drug tourists, it is often the case that the neighboring communities have not created a complementary policy to improve the situation, being satisfied to merely criticize and complain. Working together across the borders to solve this problem is rare.

Three special criminal justice policy programs can be singled out as exemplary of the Dutch trend to more vigorously assert its compliance in drug policy as a member state in the European Union: (1) the combined effort to reduce the production and trafficking of Ecstasy; (2) the comprehensive plan to reduce cocaine smuggling through Schiphol Airport; and (3) the intensified enforcement of the cannabis cultivation laws, with an emphasis on organized crime. Despite these increasingly stringent initiatives, the government still receives substantial internal and external criticism that these national policies have not been effective. Yet, the prevalence of drug use in the Netherlands is not higher, and is in fact considerably lower, than in the United States and most other European countries. Citizen groups and mothers' groups operate in many Dutch cities, organizing against the problems caused by drug users and pressuring the government for tougher policies.

Given the shortcomings of the national policy (as pointed out by its critics), most indicators show that the policy of risk reduction reinforced by targeted law enforcement and criminal justice programs is succeeding, and that drug use in the Netherlands has stabilized. A 2005 national survey of the general population (between the ages of 15 and 64) found that the percentage of those who had used drugs in the preceding year had not increased substantially since 2001, with the lifetime prevalence of having tried various drugs at least once as follows: cannabis, 5.4 percent; cocaine, 0.6 percent; amphetamine, 0.3 percent; and Ecstasy, 1.2 percent. Surveys of the school population show similar stable patterns. However, indications from the nightlife scenes are not consistent. In Amsterdam the number of emergencies for GHB, a popular club drug, have increased. The *National Drug Monitor*, an annual report that compiles data from several sources, reports an increase and a large variation in the use of cocaine by young adults in the "club scene."

COCAINE AND HEROIN

For crack cocaine and opiates, there have been no new estimates since 2001 that would indicate a change in the rate of users of 3.1 per 1,000 in the population. The 2006 estimate of these "hard drug" users indicated there were 33,499 users, with a confidence interval of between 23,773 and 46,466. Most hard drug users consume heroin and cocaine daily. While injecting drug use has been decreasing—and with it the percentage of AIDS cases and Hepatitis C attributable to injecting drug use—the prevalence of HIV is relatively high in Amsterdam (26%) and Heerlen (22%), a small city in the south of the country. The population of hard drug users is also substantial in Rotterdam (10%) and Utrecht (10%). In addition, an increase in the prevalence of psychiatric and somatic co-occurring disorders is reported in this population. Studies have found that one-third of this population suffers from major depression and that 60 percent show conduct disorders.

The demand for treatment among users of heroin and methadone has declined over the past years, according to the *National Drug Monitor*. Innovative techniques such as cue exposure therapy to extinguish cravings are available for those addicts who do present for treatment. However, notable increases in treatment demand among other groups of users have been observed. Since the indicators of drug use seem to be stable, these increases in treatment demand are likely to be due to other factors,

such as the changes in the national drug policy targeting indicated vulnerable groups and, to a lesser degree, increases in potency of drugs.

Although there was a strong growth in the number of primary cocaine users between 1994 and 2004 (from 2,500 to 10,000) this trend did not continue in 2005 and 2006. The number of amphetamine users reported by drug treatment programs is relatively limited (4% of all drugs clients in 2006) but has shown a clear upward trend since 2001. The most pronounced increase in treatment demand has been in the number of cannabis users, which rose from 1,951 in 1994 to 6,544 in 2006. The average THC concentration in Dutch home-grown marijuana peaked in 2004 (20%), leveled off in 2005 and 2006 (18%), and decreased in 2007 (16%). Considering this indicator alone, cannabis treatment demand can be expected to stabilize or decrease in the near future. In addition, vigorous prevention campaigns carried out among vulnerable populations will quite likely also contribute to a reversal in the demand for cannabis treatment. Treatment targeting vulnerable subpopulations of adolescents has adopted multidimensional family therapy approaches from the United States. (Indeed, almost every kind of drug treatment for any kind of drug problem is available in the Netherlands.)

The principle of the normalization of drug problems argues that much of the harm attributed to the use of hard drugs, such as heroin, is based on the negative definitions, stigmatization, and discrimination of society that is internalized by the hard drug users. The principle of normalization leads to multiple efforts to reintegrate the heroin user into the community and to fight against his or her stigmatization. However, this effort has been expanded not only to the negative labeling of the hard drug user by society, but also to addressing the large amount of public nuisance caused by this vulnerable population. The primary instrument to achieve these policy goals is an extensive system of methadone maintenance programs (a widely used pharmacotherapy for heroin users), which is enhanced by counseling and social service support. In addition, drug users are encouraged to organize self-help groups and mobilize for positive changes in their own subcultures.

In the mid-1990s the national government launched an ambitious experiment that prescribed heroin to an indicated group of chronic treatment-resistant heroin addicts who were not responding well to the methadone services and becoming an increasing source of public nuisance. The experiment was launched in the larger cities of the Netherlands and involved the establishment of specialized clinical facilities where heroin was prescribed. The clinically based prescription of heroin was carefully evaluated and monitored according to the highest standards of clinical management science. The results showed a resounding success, and in 2004 the Dutch government decided that the medical prescription of heroin should expand its treatment capacity from 300 to 1,000 slots. Following this expansion of treatment capacity, and after extensive deliberations, heroin became normalized through its official registration as a medicinal product indicated for chronic treatment-resistant heroin addicts. The prescription of drugs has also included medical marijuana, which is regulated by an office in the Ministry of Public Health and resembles the systems developing in several states in the United States.

LAW ENFORCEMENT INITIATIVES

Another national experiment targets the vulnerable subpopulation of hard drug users, the "prolific offenders" who especially contribute to the public nuisance problem. The experiment provides these individuals with a highly articulated form of compulsory treatment. The intervention aims at the prevention and reduction of crimes committed by drug users, since a considerable proportion of crime and recidivism in Dutch cities is attributable to this subpopulation. The experiment is consistent with the Dutch harm reduction axiom that a substantial reduction of the crime caused by this subpopulation's members could be reduced by providing a structured program of treatment and social services that addresses their addiction problems.

In 2001 the experiment known as the Court Ordered Treatment for Drug-Dependent Offenders (Strafrechtelijke Opvang Verslaafden, or SOV) was launched. The evaluation study of the SOV program found that it was more effective than regular imprisonment in terms of crime reduction, illicit drug use, and social participation. Drug users participating in SOV are engaged in a stepwise, phased reintegration program into society, with each phase lasting six to nine months. An initial closed phase (day-and-night

in SOV) is followed by a second half-open phase (extramural during daytime, in SOV during the night). Re-entry into society occurs in a final open extramural phase. In 2006 the SOV was replaced by the broader Placement in an Institution for Repeat Offenders (Inrichting voor Stelselmatige or ISD) program, which does not limit participation to men without psychiatric problems and has became a regular program within prisons.

DRUG RESEARCH AND INTERNATIONAL COOPERATION

Research in the Netherlands continues to play a pivotal role in a constant process of modification of Dutch drug policy. The experimental and scientifically based foundation of Dutch drug policy provides a persistent counterforce to tendencies in the government and civil society for moralistic redefinitions of the country's drug problems. A number of universities, along with private and governmental institutions, conduct research in all areas of drug use, with funding provided by national and city governmental agencies and private foundations. This research contributes important publications to the international scientific and policymaking communities. The joint research program of the Netherlands Organization for Health Research and Development (ZonMw) and the U.S. National Institute on Drug Abuse (NIDA) evidences the prestige of Dutch drug research. Research teams from both countries contribute to joint projects that are prioritized in joint meetings. This program has established a unique and effective forum for identifying similarities and differences in national drug-policy priorities in a historical context of profound policy differences.

Examples of some of the current joint projects that encompass representatives from all regions of the two countries include: drug prevention in schoolchildren; drug interventions in the dance club scene in Rotterdam and San Francisco; implicit cognition and early intervention; prevention of substance abuse in ADHD children; a genetic approach to opioid receptors and addiction; and analysis of the brain development of adolescent marijuana users. Yet while this research program provides a good example of the international recognition of Dutch research on drugs, it also stands in contrast with the continuing tensions and problems that Dutch drug policy, especially in the area of cannabis, has with the neighboring countries of Belgium, Germany, and France.

TOBACCO

Around 20,000 people die each year in the Netherlands as a direct consequence of the use of tobacco. Tobacco smoking in early adolescents has increased rapidly in the Netherlands. In 2005 the prevalence of tobacco use among 16 year olds was estimated at 52 percent for boys and 59 percent for girls. In 1998 a prevention platform for the selling of tobacco to youth was organized, and since 2003 the sale of tobacco to youth aged 16 or under has been prohibited. However, the effectiveness of these measures has been questioned because it has been reported that the sellers are not consistently asking for identification from those making purchases.

To increase the vigor of the public health efforts to reduce the risks, a ban on the use of tobacco in all cafes and restaurants was initiated on July 1, 2008. This measure is another example of the attempts by the Netherlands to be consistent with the norms of the European Union. Apart from changing the normal environment of Dutch public life, there has been much discussion about how this ban will affect the coffee shops. On one side is the opinion that this ban will lead to the closing of the shops, while the opposite viewpoint is that the ban is only for tobacco and does not apply to cannabis. Informal changes are already being observed in local coffee shop rules, such as only allowing pure cannabis to be smoked. Since the preferred method of smoking cannabis in the Netherlands has been in a "joint" containing a mixture of tobacco and cannabis, the tobacco ban is an example of the far-reaching affects of the tobacco ban on the formal and informal regulation of other substances.

ALCOHOL

there is widespread use of alcohol in the Netherlands, with the prevalence in the general population (individuals aged 12 years and older) put at 81 percent. While it is generally recognized that moderate use of alcohol has few health risks, alcohol abuse is seen as one of the top 10 health problems in the country. Between 2,000 and 3,000 people die

each year of alcohol abuse. The awareness of the health risks of alcohol has been substantially increased through public discussion about the role of genetic vulnerability to alcohol problems and what the policy consequences of this new knowledge should be. In November 2007, the government issued its " Main Line Alcohol Policy Letter," in which the priority goal of the nation's alcohol policy was held to be the prevention of harmful alcohol use. The most important target group for this policy is youth. The new policy recommends vigorous measures that will prevent children and adolescents from using alcohol before the age of 16.

However, the existing data since 1984 show that there have only been slight fluctuations in the use of alcohol among the school population. Measurements show a slight decrease in lifetime prevalence, from 85 percent in 2003 to 79 percent in 2007. Nevertheless, research has led to recommendations that parents more actively attempt to delay the onset of alcohol use in their children.

The focus on the family has been combined with special attention to alcohol use at work, in the club scenes, and while driving. More attention is also being given to the control of the selling of alcohol to youth. For example, it is now required that identification be shown before purchasing alcohol and for entrance to clubs where alcohol is served. However, the consequences of these policy requirements are not yet known.

See also **Cannabis; Club Drugs; Coca/Cocaine, International; Coerced Treatment for Substance Offenders; European Union; France; Germany; Harm Reduction; Heroin; International Control Policies; Marijuana (Cannabis); Methadone Maintenance Programs; Needle and Syringe Exchanges and HIV/AIDS.**

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BERT BIELEMAN

NEUROLEPTIC. Neuroleptic includes any of a group of drugs that are also called antipsychotics. Neuroleptics are used as medications in the treatment of acute psychoses of unknown origin, including mania and schizophrenia. The prototype neuroleptic drugs are chlorpromazine (Thorazine), haloperidol (Haldol), clozapine (Clozaril), lithium (Lithonate), and thioridazine (Mellaril). Some of the newer drugs include risperidone (Risperdal), quetiapine (Seroquel), and olanzapine (Zyprexa). The site of action for these drugs (receptor site) is the central nervous system where they produce antipsychotic effects.

These drugs are also used for antianxiety, although other agents are more effective and do not have the long-term side effects that neuroleptics do. Drug therapy alone is not entirely effective in treating psychoses, and it is used in combination with acute and long-term support and medical care. Some neuroleptics are also used in the treatment of nausea, vomiting, alcoholic hallucinosis, neuropsychiatric diseases marked by movement disorders (e.g., Huntington's disease and Gilles de la Tourette's syndrome), pruritus, and intractable hiccough.

See also **Schizophrenia.**

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GEORGE R. UHL
VALINA DAWSON

NEURON. The gross anatomy of the central nervous system—the brain and spinal cord—was studied in some detail during the seventeenth and eighteenth centuries, but not until the nineteenth century did scientists begin to appreciate that the central nervous system (CNS) was composed of many millions of separate cells, called neurons (also called nerve cells). This discovery had to await technical improvements in the microscope and the

development of specialized stains that permitted scientists to observe the microscopic anatomy of the nervous system.

HISTORY

In the 1870s, the Italian anatomist Camillo Golgi developed such a special staining technique, and he and other scientists were then able to observe under the microscope the fine structures of the cells of the nervous system. Yet Golgi may not have fully appreciated that what seemed to be an extended network of nerve tissue were in reality millions of distinct neurons with fine fibrils touching each other. It was the Spanish scientist Santiago Ramón y Cajal who was credited with expounding the neuron theory. In 1906, Golgi and Ramón y Cajal shared the Nobel Prize in physiology/medicine for their discoveries on the nature of the nervous system.

Even after the concept of separate neurons was generally accepted, there was controversy for many years about how the separate neurons communicated with each other. At the end of the nineteenth century, many scientists believed they did so by means of electric impulses. Others believed there was a chemical messenger that allowed neurons to influence each other. Around 1920, acetylcholine was discovered, the first of many nerve messengers that would be discovered during the subsequent decades.

FUNCTION

The neuron is the basic functional cellular unit of nervous system operations; it is the principal investigational target of research into the actions of addictive drugs and alcohol. An essential feature of the cellular composition of the brain is the high density of extremely varied, heterogeneously shaped neuron groups (see Figure 1). To understand the specialized aspects of neurons and their function, therefore, requires a discussion of the general structural and functional features characteristic to all neurons and the degree to which unique variations form consistent subsets of neurons.

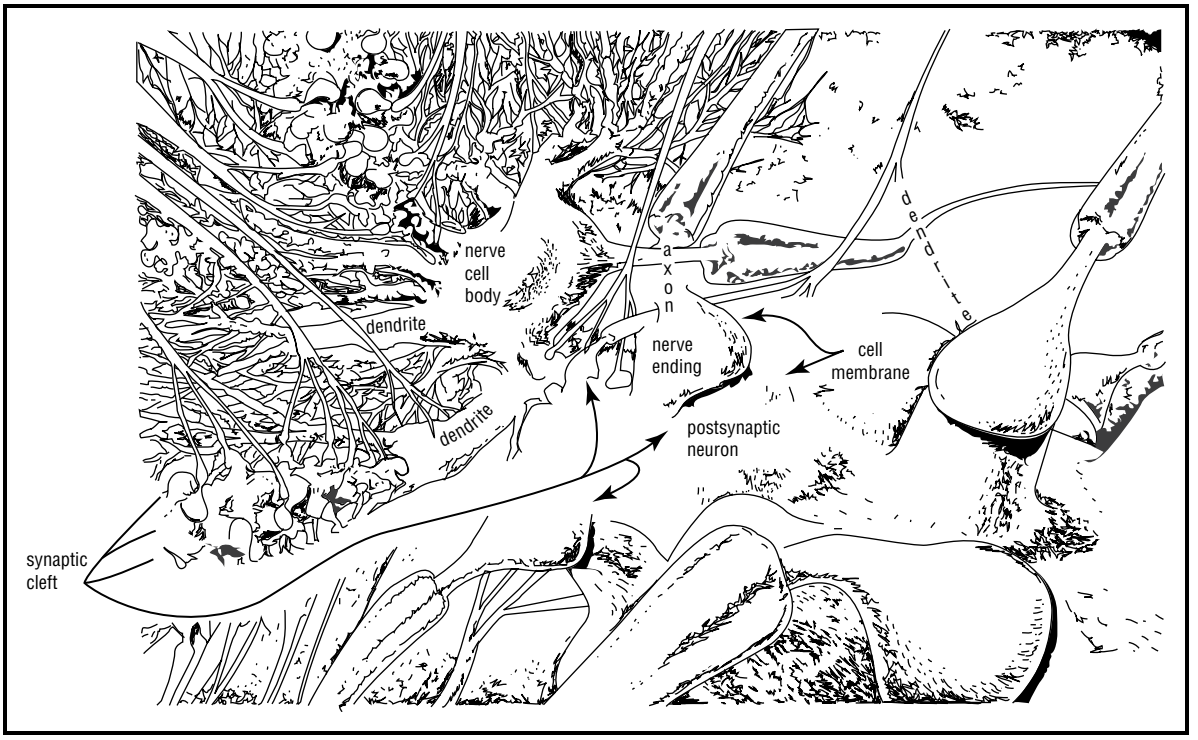

Figure 1. Neuronal complexity. The complexity of the neuronal network in the brain is demonstrated by this bundle of neurons, which form a vast and ramified structure with their cell bodies, outgrowths, and intercellular contact points. (Modified from Figure 1, in M.J. Kuhar's Introduction to Neurotransmitters and Neuroreceptors in *Quantitative Imaging*, edited by J.J. Frost and H.N. Wagner. Raven Press, New York, 1990.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

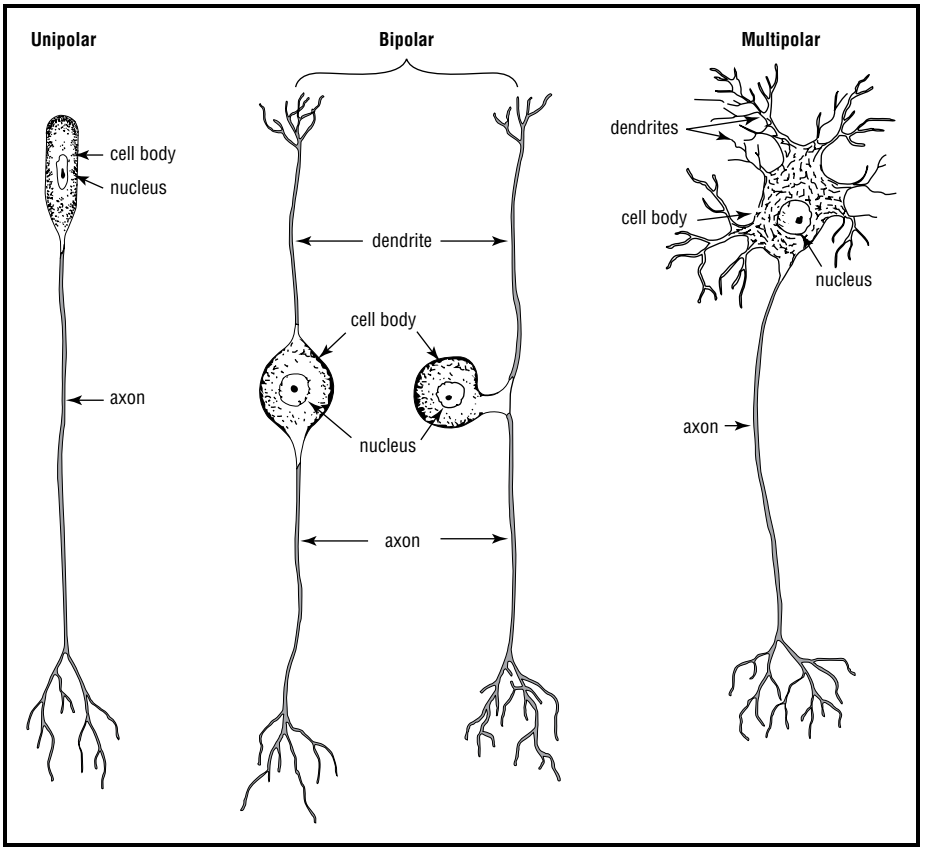

Figure 2. Three types of neurons. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Neurons share many cellular properties that distinguish them significantly from other cell types in other tissues; those changes within the cell's regulatory processes of greatest interest to researchers of addictive drugs, however, depend on features that form distinctions within the class of cells called neurons. Furthermore, the assembly of individual neurons into functional systems, through highly precise circuitry employing highly specified forms of chemical interneuronal transmission, allows for the sensitivity of a brain to addictive drugs.

In some organs of the body—such as the liver, kidney, or muscle—each cell of the tissue is generally similar in shape and function. Within that tissue, all perform in highly redundant fashion to convert their incoming raw material into, respectively, nutrients, urine, or contractions, which establishes the function of the specific tissue. In the nervous system, the variously (heterogeneously) shaped neurons (see Figure 2), supported by an even larger class of similarly (homogeneously) shaped non-neuronal cells, termed *neuroglia*, convert information from external or internal sources into information ultimately integrated into programs for the initiation and regulation of behavior.

This integrative conversion of sensory information into behavioral programs results from the rich interconnections between neurons, and it depends on the extremely differentiated features of neurons—their size and shape; their extended cell-surface cytoplasmic processes (dendrites and axons); and their resultant interconnections that establish the sources of their incoming (afferent) information and the targets of their outgoing (efferent) communication (see Figure 3).

COMMON FEATURES

As cells, neurons share some features in common with cells in all other organ systems (see Figure 4). They have a *plasma membrane* acting as an external cell wall to form a distinct boundary between the environment inside (intracellular) and outside

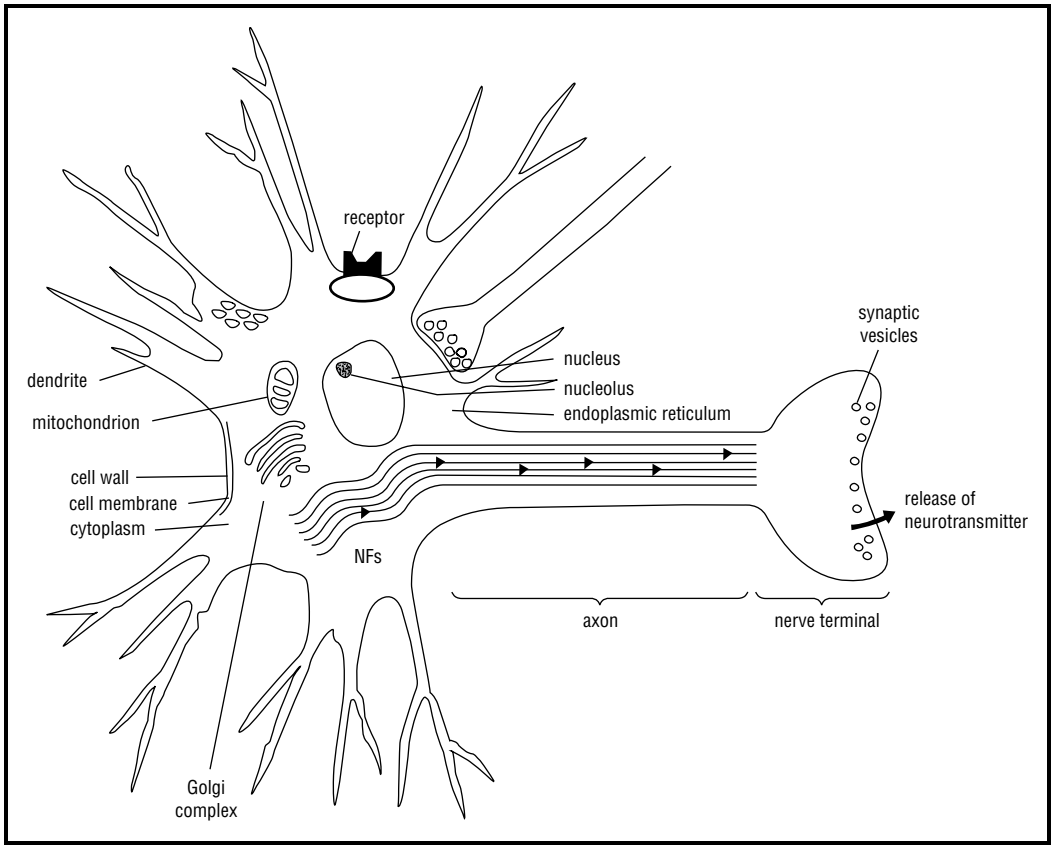

Figure 3. Features of the neuron. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

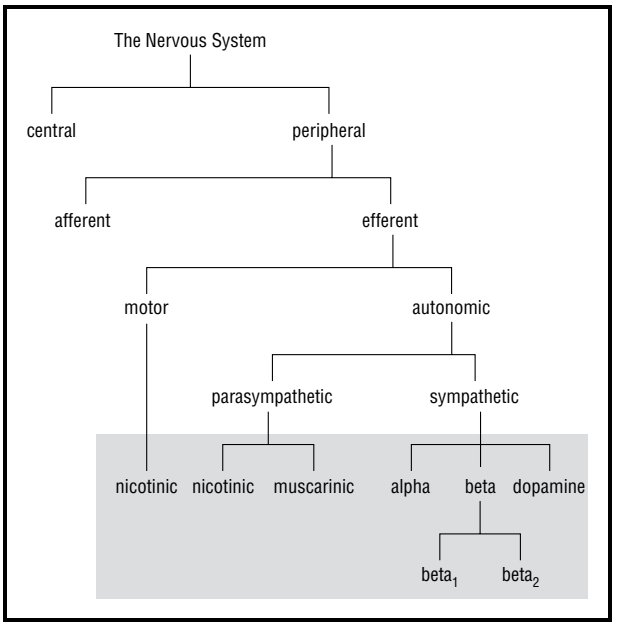

Figure 4. Relationship of receptor types. Efferent nerves in the peripheral nervous system. (Receptor subdivisions for alpha and dopaminergic receptors are not included.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

(extracellular) the cells. The intracellular material enclosed by the plasma membrane is termed *cytoplasm*. Like all other cells (except red blood cells), neurons have numerous specialized intracellular organelles, which permit them to maintain their vitality while performing their specialized functions.

Thus, neurons have *mitochondria* (singular, mitochondrion), by which they convert sugar and oxygen into intracellular energy molecules, which then fuel other metabolic reactions. Neurons have abundant *microtubules*: thin intracellular tubular struts by which they form and maintain their often highly irregular cell structure. Neurons are also rich in a network of intracellular membranous channels, the *endoplasmic reticulum*, through which they distribute the energy molecules, membrane components, and other synthesized products required for functioning. Like other cells that must secrete some of their synthesized products for functioning, as neurons do with their neurotransmitters, some parts of the endoplasmic reticulum, such as the *smooth endoplasmic reticulum*, are specialized for

the packaging of secretion products into storage particles, which in neurons are termed *synaptic vesicles*. At the center of the pool of cytoplasm, neurons possess a *nucleus*, which, as in other nucleated cells, contains the full array of the genetic information characteristic of the individual organism. From this nucleus, selected subsets of genetic information are expressed to provide for the general shared and the specific unshared features of the cell. The nucleus of the neuron cell is enclosed within a membranous envelope that, as in many other types of cells, exhibits multiple nuclear pores through which information can be conveyed to and from the nucleus.

UNIQUE FEATURES

The plasma membrane of neurons differs from that of non-neuronal cells in that it contains special proteins, termed *voltage-sensitive ion channels*. Such channels are conceptually small tubular proteins embedded in the membrane of the neuron, which, when activated under specific conditions, allow positively charged ions of sodium, potassium, and calcium to enter the neuron. The existence of such electrically sensitive channels permits the neuron to become electrically excitable. The expression and selective distribution (compartmentalization) of such electrically excitable channels along its efferent processes, the axons, permit neurons to conduct signals efficiently for long distances; this also accounts for the bioelectrical activity of the brain assessed by *electroencephalography (EEG)*. Similarly, the distribution of such electrically excitable ion channels along the receptive surfaces of the neurons (its dendrites and cell body [soma]) allows them to conduct and integrate signals from all over the extended shape of the neuron.

The smooth endoplasmic reticulum of the neuron is somewhat more elaborate and extensive than other cells that secrete their products; this specialized and extensive smooth endoplasmic system is termed the *Golgi complex* (or *Golgi apparatus*). Discovered accidentally, it was a useful marker for staining the nervous system to distinguish neurons from other cells of the brain when under inspection by microscope.

The nucleus of neurons is often highly elaborated, with multiple creases or infoldings, exhibiting complex configurations, within which are typically dense accumulations of cytoplasmic organelles, and almost always a very distinctive intranuclear clustering of genetic material, the *nucleolus*. Differentiated neurons—neurons whose developmental stage is past the step at which cell-type dedication has occurred—are unable to undergo cell division, in distinct contrast to comparably metabolically active cells in such complex tissues as liver, kidney, muscle, or skin. As a result, mature neurons can repair themselves, up to a point, but are unable to regenerate themselves or respond to their growth factors in a manner that would in other tissues lead to cell division and replacement.

The most distinctive cellular feature of neurons is the degree to which they express unique patterns of size and shape. In mammals, all neurons have highly irregular shapes; such shape variations are categorized in terms of the number of cell surface extensions, or neuronal processes, that the neuronal subset expresses, as in Figure 2.

Some neurons have only one cellular process extending from the surface of a round or nearly round cell body; this form of neuron, a *unipolar* neuron, is typical of invertebrate nervous systems. Typical unipolar neurons are the cells of the dorsal root ganglia, in which a single efferent axon conducts information toward or away from the cell body through a branched axon.

Most neurons of the central nervous system of mammals are multipolar. That is, in addition to the efferent axon, which may also have many subsets of secondary axons, called *collateral branches*, that stem from the main efferent process axon, elaborations may also be expressed from the cell body surface. The latter elaborations are termed *dendrites*, because their shape resembles the limbs of trees. Dendrites protrude from the cell body, and they, as well as the cell body, constitute the receptive surfaces of the target neuron onto which the afferent connections make their synaptic connections.

DISTINGUISHING NEURONS

Since neurons come in so many shapes and sizes, early investigators of the brain sought to make distinctions among them, based in part on their locations, their sizes and shapes, and the connections they could be shown to receive or emit. Every scientist who worked in the formative era of brain

research sought to describe a unique subset of neurons that were forever after named for their initial describer or the unique property defined. Thus, we have *Betz neurons*, large layer V–VI neurons of the motor cortex, and *Purkinje neurons*, the major output neurons of the cerebellar cortex, as well as neurons named for their shapes and appearance—*pyramidal neurons* of the cerebral and hippocampal cortices, *mitral* and *tufted neurons* of the olfactory bulb, and *granule cell neurons* of the cerebellar, hippocampal, and olfactory cortices. The last mentioned have relatively compact cell bodies, densely packed together, giving the brain a granular appearance by optical microscopy.

Dendrites and axons exhibit highly distinctive morphological patterns. The surfaces of dendrites and axons can be distinctive in the shapes of their branches. This permits fine discrimination among neurons (stellar, or star-shaped, neurons; chandelier neurons; or mossy or climbing axon fibers). Some neurons exhibit dendrites whose surfaces are smooth (aspiny); others are highly elaborated (spiny), which may serve to enlarge the receptive surfaces and enhance the degree to which such neurons may integrate afferent information.

Similarly, the morphology and stability of the axons may also be highly variable. Some neurons direct their axons to highly constrained targets in a more or less direct route; others may be highly branched, with multiple collateral branches to integrate communications from one cell cluster to many divergent targets. To provide the essential support of anabolic and secretory materials within these highly elaborated cellular structures, neurons have evolved an efficient form of intracellular transport, an energy-dependent, microtubule-guided, centripetal and centrifugal process by which organelles are dispensed to and returned from the distal processes (as well as probable macromolecular signals sensed by pinocytotic-like [fluid uptake] incorporation of such signals by distal dendrites and axons). Such signals may serve as local growth-regulatory factors, allowing even the nondividing neurons to alter their shape and connections in response to activity and signals received from their afferent sources.

NEURONAL IDENTITY

An individual neuron may be referred to on the basis of its size (magnocellular, parvicellular). A layer or "nuclear" cluster of neurons may be referred to by shape (pyramidal, mitral), the morphology of its axon terminals (i.e., *basket cells*, whose axon terminals make basket-shaped terminations on their targets), and its position in a sensory or motor circuit. In the latter classification scheme, those neurons closest to the incoming sensory event or to the outgoing motor-control event are termed *primary sensory* or *motor* neurons, respectively, whereas neurons at more distal positions of circuitry from the primary incoming or outgoing event are termed *secondary, tertiary*, and so on, depending on their position in that hierarchy.

In addition to these morphological qualities, neurons may also be separately distinguished on the basis of the functional systems to which they are connected (visual, auditory, somatosensory, proprioceptive, attentional, reinforcing, etc.) and on the basis of the neurotransmitters they employ to communicate with the neurons to which they are connected (cholinergic, adrenergic, GABAergic, etc.). Each of those features provides for a multidimensional definition of virtually every neuron in the brain.

See also **Brain Structures and Drugs; Neurotransmission; Neurotransmitters; Receptor, Drug; Reward Pathways and Drugs.**

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FLOYD BLOOM

NEUROTRANSMISSION. Neurons (nerve cells) communicate chemically by releasing and responding to a wide range of chemical substances, referred to in the aggregate as neurotransmitters. The process of *neurotransmission* refers to

this form of chemical communication between cells of the central and peripheral nervous system at the anatomically specialized point of transmission, the synapse (synaptic junctions). Thus, it is convenient to conceive of "the" neurotransmitter for a specific instance of synaptic connections between neurons in one brain location (the source neurons) and their synaptic partner cells (the target neurons) in another neuronal location. For example, the phrase "dopaminergic neurons of the nigro-accumbens circuit" refers to the dopamine-transmitting synaptic connections between the brain neurons of the substantia nigra and their targets in the nucleus Accumbens. Current concepts of neurotransmission, however, require a broader view; they would consider as neurotransmitters all the chemical substances that a given neuron employs to signal the other neurons to which it is anatomically connected (its synaptic targets) and through which that neuron may also be able to influence other neuronal and non-neuronal cells in the adjacent spatial environment of its circuitry (nonsynaptic targets).

In some cases—more frequent in invertebrate nervous systems, in more primitive vertebrates, and in the embryonic nervous system than in the adult mammalian nervous system—neurons may also communicate "electrically," by direct ionic coupling between connected cells, through specialized forms of intercellular junctions referred to as "gap junctions," or *electrotonic junctions*. Such electrotonic transmission sites are of relatively little direct concern to the actions of addictive drugs and alcohol. In contrast, it is the more pervasive process of chemical neurotransmission that underlies the main molecular and cellular mechanisms by which addictive drugs act—and through which the nervous system exposed to such drugs undergoes the adaptations that may lead to dependence, Habituation, withdrawal, and the more enduring changes that persist after withdrawal from the once-dependent state.

The critical characteristic of a substance designated as a neurotransmitter is the manner in which it is made and secreted. To qualify as a neurotransmitter, the release of the substance must be coupled to neuronal activity according to two rather stringent functional rules (see Figure 1).

1. The transmitter substance must be synthesized by the transmitting neuron. In most cases, the substance is made well in advance and stored in small organelles (synaptic vesicles) within the terminal axons of the source neuron, ready for eventual release when called upon.
2. The transmitter substance must be released by that neuron through a special form of activity-dependent, calcium ion (Ca^{2+})-selective, excitation-secretion coupling. Substances released through other nonactivity-coupled and non-Ca^{2+}-coupled mechanisms may be regarded as excretion (as with metabolic byproducts to be degraded), rather than secretion.

The synaptic junction is the site at which the axons of the source neuron physically make most intimate contact with the target neuron to form an anatomically specialized junction; concentrated there are the proteins that mediate the processes of transmitter release (from the presynaptic neuron) and response (by the postsynaptic neuron). Indirect evidence for some neurotransmitter systems has suggested to some scientists a general concept of *non-synaptic* interneuronal communication, sometimes also referred to as *paracrine* or *volume-transmission* communication, in which the neurotransmitter released by a designated set of presynaptic terminals may diffuse to receptive neurons that are not in anatomic contact. The sets of chemical substances that neurons can secrete when they are active can also influence the non-neuronal cells, such as the cells of the vascular system (the glia) and the inflammatory-immune cells (the microglia).

The activity of neurons can also be modified by substances released from the non-neuronal cells of the central or peripheral nervous system, substances often termed *neuromodulators*. This same term, however, is frequently applied to the effects of neuron-produced transmitter substances whose mechanisms of action and whose time course of effect differ from those of the classic junctional neurotransmitter acetylcholine.

The current research on neurotransmitters and neuromodulators pertinent to drugs and alcohol is devoted to (1) understanding how exposure to addictive drugs may regulate the genes that control the synthesis, storage, release, and metabolism of known neurotransmitters; (2) identifying new substances that may be recognized as neurotransmitters, whose effects may be related to the effects of or reactions to addictive drugs and alcohol; (3) understanding the molecular events by which neurons and other cells

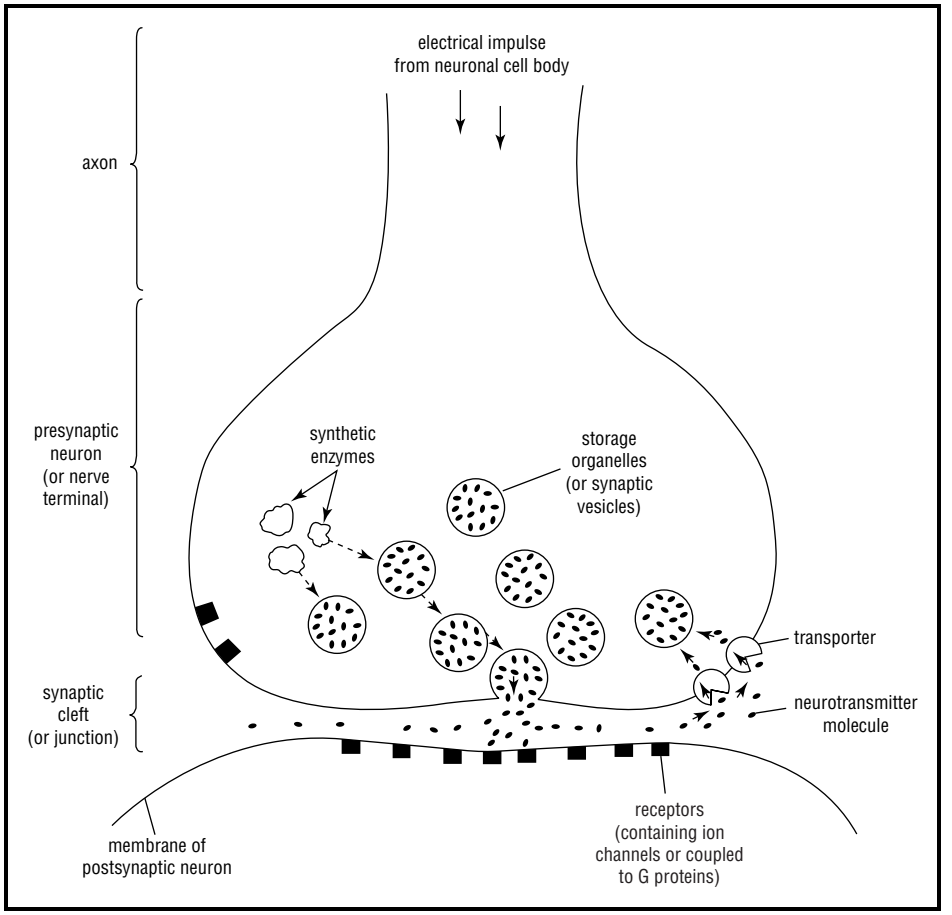

Figure 1. Synapse. Nerve ending from one neuron forms a junction, the synapse, with another neuron (the postsynaptic neuron). The synaptic junction is actually a small space, sometimes called the synaptic cleft. Neurotransmitter molecules are synthesized by enzymes in the nerve terminal, stored in vesicles, and released into the synaptic cleft when an electrical impulse invades the nerve terminal. The electrical impulse originates in the neuronal cell body and travels down the axon. The released neurotransmitter combines with receptors on postsynaptic neurons, which are then activated. To terminate neurotransmission, transporters remove the neurotransmitter back into the nerve terminal that released it. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

react to neurotransmitters in both short-term and long-term time frames (a process often termed *signal transduction*, which cells of the nervous system share with most other cells of the body) and how these processes may themselves be perturbed by the influence of addictive drugs and alcohol; and (4) understanding the operations of neuronal communication in an integrative context of the circuits that release and respond to specific transmitters, and the way in which these neuronal circuits participate in defined types of behavior, either normal or abnormal.

NEUROTRANSMITTER ORGANIZATION

There are three major chemical classes of neurotransmitters.

1. *Amino acid transmitters*: glutamate (GLU) and aspartate are recognized as the major excitatory transmitting signals; gamma aminobutyrate (GABA) and glycine are the major inhibitory transmitters. These transmitter substances occur in concentrations of one millionth part per milligram (μM/mg) protein. Since they are considered the most frequently employed transmitter substances, they have been linked to many aspects of the actions of addictive drugs.
2. *Aminergic transmitters*: acetylcholine, epinephrine (also called adrenaline), norepinephrine (also called noradrenaline), dopamine, serotonin, and histamine. The aminergic neurons constitute a minor population of neuronal

transmission sites, as reflected in the fact that their concentrations in the brain are roughly 1/1000th that of the amino acid transmitters or one billionth part per milligram (μM/mg protein). Because of their divergent anatomy (a few clusters of aminergic neurons may project onto literally millions of target neurons in many locations of the brain) and the ability of their synaptic signals to produce long-lasting effects, the aminergic neurons represent a very powerful subset of transmission conditions that is important to the effects of addictive drugs. Of particular relevance are the dopaminergic neurons—for their pertinence to the sites of reward for stimulants, opiates, and certain aspects of ethanol (alcohol) action—and the noradrenergic and serotonergic neurons—for their association with the phenomena of drug adaptation and tolerance.

3. *Neuropeptides*: of which there are dozens. Peptides are molecules containing a specific series of 2–50 amino acids, chemically arranged in a specialized "head-to-toe" chemical linkage known as a peptide bond. The order and number of the linked amino acids determine the linear structure of the peptide. In the nervous system, peptides, in general, occur in still lower concentrations than do the two prior classes of transmitter, namely at 10–100 trillionth part per milligram (pM/mg) protein. A revolutionary finding has emerged here in concepts of brain system interactions: It would now seem that neuropeptides are almost certainly never the sole signal to be secreted by a central neuron that contains such a signaling molecule, but rather accompany either an amino acid or an amine transmitter (at intrasynaptic terminal concentrations a thousand to a millionfold higher), such sites may even contain a second or third peptide as well.

Neuropeptides are of interest to the molecular and cellular mechanisms of addictive drug and alcohol action, because they may provide the postsynaptic receptors through which the drugs act (as in the case of the opiates and possibly the case for the natural benzodiazepines) or modify the effects of the presynaptic transmitters (as in the case of the peptide cholecystokinin that accompanies some forms of dopaminergic transmission, through which stimulants act and may modify responses to that amine if cosecreted).

Because of the ability to read the linear sequences of the amino acids, it has become clear that many of the neuropeptides share select small sequences and thus conceptually constitute "families" of peptides. For example, the opioid peptides all share one or more repeats of the amino-acid sequence tyrosine-glycine-glycine-phenylalanine; thus, each of the opioid-peptide genes leads to the expression of a different pre-prohormone by different sets of neurons of the central and peripheral nervous system. The existence of the shared amino-acid sequences implies that at some point in evolution, there may have been only one opioid-peptide signal, which was then duplicated and modified for use by the increasing number of neurons that came with the evolution of the mammalian brain. Such family relationships also exist for other peptide families (oxytocin/vasopressin; the tachykinin peptides; the secretin/glucagon-related peptides; the pancreatic polypeptide-related peptides), whose amino-acid sequences have shown great conservation over large domains of the evolutionary tree, attesting to the high signal quality of these molecules and the transductive mechanisms of their receptors. Other peptides, such as somatostatin and gonadotropin-releasing hormone, have no known family relationships as yet—but the discovery process here is probably not complete.

OTHER TRANSMITTER CANDIDATES

Other kinds of molecules may also be made within neurons to play auxiliary roles in intercellular transmission in the nervous system—from purines like adenosine triphosphate, lipids like arachidonic acid and prostaglandins, and steroids similar to those made and released by the adrenal cortex and the gonads. These substances may, in some cases, act as intracellular second messengers to underlie the effects of the aminergic and peptidergic transmitters (see below); they therefore have implicit relevance to the effects of the addictive drugs whether or not they may also serve as primary transmission signals.

Investigators have revealed that under some conditions active neurons may synthesize gaseous signals, such as nitric oxide and carbon monoxide, which can carry rapidly evanescent signals over

short distances. The effects of these transmission-related substances will undoubtedly become of increasing importance to the explanations of the mechanisms of action or adaptation to the addictive drugs.

SIGNAL TRANSDUCTION ORGANIZATION

Aside from the chemistry of the neurotransmitter substances, further insight into their role in the actions of addictive drugs arises from the viewpoint of their synaptic physiology and their underlying mechanisms of signal transduction. When neurons respond to neurotransmitters, the ultimate changes in the excitability and metabolic activity of the responding neuron generally require changes into or out of the cell in the flow of ions (natural chemical elements of the extracellular fluid)—some with positive charge (sodium, potassium, and calcium) and others with negative charge (chloride).

As a general rule, it would appear that every neurotransmitter has more than one form of postsynaptic receptor through which its effects are mediated. Before the ability to characterize these receptors through molecular genetics, such receptor subtypes were identified on the basis of the comparative pharmacological potency of synthetic agonists or antagonists of the natural transmitter. With the advent of molecular cloning, however, an even finer subtyping would appear to be required, since many of the conclusions on receptor pharmacological patterns were based on analyses of tissue fractions that undoubtedly contained many molecular forms. A major effort in the future will be to link more explicitly the molecular and pharmacological characterization of neurotransmitter receptor subtypes and to determine which of them are most critical to the effects of, and adaptations to, addictive drugs.

Three major formats have been revealed for the transductive process.

1. *Directly regulated ion channels.* Here the ion channel to be opened is formed by the units of the receptor molecule itself, as recently established by direct cloning of several such receptorionophores. Such receptors are now known to be the motif of the nicotinic-cholinergic receptors of the neuromuscular junction and the central nervous system, as well as for the three types of glutamate receptor, the several isoforms of the GABAA receptor, the glycine receptor, and at least one form of a serotonin receptor.

   Common features of these receptors are (a) they are composed of several (3–5) subunits, called monomers, that apparently may be combined in differing ratios (so-called multimeric recombinations) by various neurons to constitute the "holoreceptor"; (b) each monomer consists of four presumed transmembrane domains; and (c) discrete sections of the receptor monomer, either within the membrane or the cytoplasm, account for their voltage and chemical sensitivity, and for the ease and duration of openings in the ion channel.

2. *Indirectly regulated ion channel-receptors.* This form is based on the similarities between the visual pigment rhodopsin—the molecule used by photoreceptor neurons (rods, cones) to transduce light into signals to other neurons of the retina—and the beta-adrenergic receptor—one of the types of receptors regulated by the amine norepinephrine. This general form of transducing molecule was later found to be the form also used by the cholinergic muscarinic receptor, as well as by most serotonin and all known dopamine receptors, plus all the known peptide receptors.

   The common features of this class are (a) the receptor is a single molecule, with seven transmembrane domains; (b) activation of these receptors by their signaling molecules leads to further interactions of the receptor with other large proteins, some of them enzymes, within or near the plane of the membrane; and (c) the eventual indirect regulation of the ion channel, either the opening or closing of the channel, is then mediated through small molecular intracellular second messengers, such as the calcium ion (Ca^{2+}) or the products of the associated enzymes, yielding intracellular second-messenger molecules, such as cyclic adenosine monophosphate (cAMP), or a lipid such as an inositol phosphate, diacyl-glycerol, or an arachadonic acid catabolite. The essential common second step of such transduction cascades is that the activated receptor interacts with a guanosine triphosphate (GTP)-binding protein (termed a *G-protein*) composed of three monomer subunits. The G-protein complex dissociates to activate the enzyme making the second

messenger and, at the same time, hydrolyses the GTP and reassociates to end the cycle of signal generation. The second messenger consequences of this form of transduction, however, may be more enduring—activating one or more enzymes (protein kinases or phosphatases) that can add or remove phosphate groups on structural proteins or other enzymes, to activate or inactivate them. Such events can significantly shift the metabolic state of the responding cell and eventually regulate the expression of its specific genes. One such gene target is the immediate early genes of the nervous system, the protooncogenes, discovered some years ago because of the mutated forms used by oncogenic viruses, which induce cancer in non-neuronal cells.

3. *The receptor-enzyme*. This third major molecular motif of signal transduction has been elucidated recently; although it is already clear that this form does exist in the mammalian brain, it has been studied more in non-neuronal systems. This motif's characteristics are that the receptor for some peptides is itself the enzyme guanylate cyclase, which is directly activated by receptor-ligand binding, leads to an intracellular generation of cyclic guanosine monophosphate, and then to a cascade of events similar to that described for AMP.

SYNAPTIC INTERACTIONS

Most neurons receive synaptic input simultaneously from hundreds of other neurons, each of which employs its own mix of transmitters. The transductive processes underlying these individual events can influence the intensity and duration of the subsequent responses, thereby integrating incoming signals and providing the basis by which activity in assemblies of interconnected neurons results in behavioral output by the brain.

To gain insight into the basis by which the events of neurotransmission can lead to multineuronal programs of interaction, such as those required to initiate responding for an addictive drug, requires knowledge both of the anatomical substrate over which such programs of neuronal activity take place and of the effects of the neurotransmitters at each of the cellular elements of such an interactive ensemble of neurons.

See also **Addiction: Concepts and Definitions; Brain Structures and Drugs; Limbic System; Tolerance and Physical Dependence.**

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NEUROTRANSMITTERS.

A neurotransmitter is any chemical substance (the first recognized was acetylcholine) that neurons (nerve cells) secrete to communicate with their target cells (glands, muscles, and other neurons). Neurotransmitters diffuse from their sites of release—from the presynaptic nerve terminal—across the synaptic cleft, to bind to receptors on the external surface of the postsynaptic cell. Activation of these receptors allows for the transmission of commands (excitation, inhibition, and other more complex forms of regulation) from the presynaptic neuron to the postsynaptic cell.

A neurotransmitter is released from a nerve ending, interacts with specific receptors, and is then either transported back into the presynaptic neuron

or destroyed by metabolic enzymes in the synaptic cleft.

Chemically, neurotransmitters are amino acids, amines, or peptides. Peptide transmitters commonly coexist and may be cosecreted with amino acid or amine transmitters.

See also **Dopamine; Endorphins; Neurotransmission; Norepinephrine; Serotonin.**

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NEW YORK STATE CIVIL COMMITMENT PROGRAM. The New York State Civil Commitment Program was the largest and most expensive drug treatment program of its kind during the 1960s and 1970s. Modeled after the California Civil Addict Program (CAP), it was established in the early 1960s in response to the dramatic rise of New York's heroin-addict population. The first reaction to the problem was expressed in the Metcalf-Volker Narcotic Addict Commitment Act of 1962, which sent arrested addicts to state mental-hygiene facilities for treatment. The total failure of this program prompted New York Governor Nelson Rockefeller to substantially modify and expand the program in 1966 by creating a Narcotic Addiction Control Commission (NACC). NACC was established to administer the New York State Civil Commitment Program, which involved a major statewide network of residential treatment centers.

Six different types of centers handled the following phases of treatment: examination and detention; detoxification, orientation, and screening; residential treatment and rehabilitation; temporary return; indefinite return; and halfway houses. Those who were eligible for treatment at a center included addicted individuals who had been arrested or convicted for a felony or misdemeanor, who had been involuntarily committed by their family or a friend, or who had volunteered to be treated. The treatment process consisted of a period of commitment within the institution, followed by community aftercare. Clients were under the control of the agency for an average of twenty-five months, of which ten months was spent in residence at the institution (Winick, 1988).

THE PROGRAM'S DEMISE

The program reached its peak in 1970 when twenty-four state facilities with 4,100 beds and a staff of over 5,000 provided services to 6,600 addicts. Followup studies of the program at this time were few, but they tended to indicate some positive outcomes (Winick, 1988). After 1970, the program began to lose public support and became a regular political target because of charges of cost overruns, allegations of staff brutality, and questionable administrative procedures (Winick, 1988). There was also a general change in philosophy that drew politicians away from supporting state-run institutions and toward recommending community-based treatment. In addition, political leaders began to move away from rehabilitation and toward harsh criminal sanctions for persons possessing or selling narcotics.

Governor Rockefeller announced in 1971 that he had lost confidence in the New York program and initiated a two-thirds cutback in budget and clients. The number of occupied beds steadily diminished because of these cuts and by 1979 the last two centers shut down (Winick, 1988). From 1966 to 1979, the program had cost approximately $1 billion. By the time the program was closed, each resident was costing an average of $29,000 per year, as compared with $8,500

for a resident in a therapeutic community and $14,500 for a prison inmate (Winick, 1988). In 1980, the state legislature repealed the civil commitment law.

WHY THE PROGRAM FAILED

Poor planning played a major part in the failure of the program (Winick, 1988). Due to political pressure, the first eight facilities opened in less than a year. Staffing was an immediate problem. The directors of the treatment facilities had inadequate administrative or clinical experience, since they were mostly political and civil service appointees (Inciardi, 1988). Facilities also were ill chosen and they too contributed to staffing deficiencies. NACC purchased underused prisons from the New York Department of Corrections and used them as treatment facilities. Many of the former prison guards were maintained as rehabilitation officers who performed both a counseling and custodial function. These officers were inadequately trained for their new positions, and they often disciplined program participants too harshly (Inciardi, 1988). The result was an environment that did not offer therapeutic benefits and was not conducive to behavioral change.

The screening of candidates for the program, moreover, was not consistent, and the criteria for completion of the program were ambiguous. The reentry and aftercare programs were equally ill equipped to handle the task at hand. The aftercare "officers" had no authority to arrest a client for violation of aftercare conditions, and their caseloads were too large to allow close supervision. As a consequence, a great number of parolees fled or stopped reporting (Winick, 1988).

Apart from programmatic failings, the civil commitment program began just as political leaders started to move away from rehabilitative models. Governor Rockefeller provides a telling example. By the early 1970s, when heroin addiction showed no signs of abating, Rockefeller decided that the criminal justice system should be directed more forcefully at drug users. In 1973, a group of statutes, popularly known as the Rockefeller laws, went into effect. These laws imposed mandatory prison sentences on those that possessed or sold drugs. These sentences, even for first-time offenders, were very long. Repeat offenders could receive life imprisonment. With the Civil Commitment Program unable to produce reliable and cost-effective results, the impulse to incarcerate drug users proved almost irresistible.

See also **Civil Commitment; Coerced Treatment for Substance Offenders; Narcotic Addict Rehabilitation Act (NARA); Prisons and Jails; Rockefeller Drug Laws.**

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NFLIS. *See* **National Forensic Laboratory Information System (NFLIS).**

NICOTINE. This is a psychoactive chemical substance found in tobacco products, including cigarettes, cigars, pipe tobacco, and smokeless tobacco such as chewing (spit) tobacco and oral and nasal snuff. The nicotine molecule is composed of a pyridine ring (a 6-membered nitrogen-containing ring) with a pyrrolidine ring (a 5-membered nitrogen-containing ring).

Nicotine can occur in two forms. The active form, called L-nicotine, is found in tobacco plants of the genus *Nicotiana*. These are chiefly South

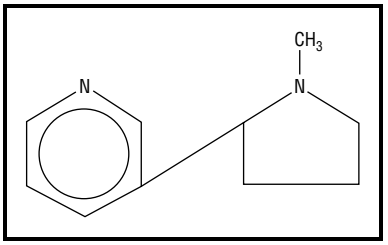

Figure 1. Chemical structure of nicotine. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

American plants of the nightshade family (*Solanaceae*)—annuals cultivated since pre-Columbian times for their leaves, especially *Nicotiana tabacum*. The inactive form, D-nicotine, is not present in tobacco leaves but is formed, to a small extent, in the combustion of tobacco during smoking. These two forms are stereoisomers, meaning that even though they are both nicotine, they have different three-dimensional structures. In pure form, nicotine is a colorless liquid, but it turns brown on exposure to air.

Nicotine is water-soluble and transfers from tobacco to cigarette smoke readily, because it vaporizes easily. Once it is in the body, conditions are ideal for rapid distribution to blood and tissues because nicotine is a weak base, and when un-ionized under alkaline conditions, such as those found in the blood stream, it crosses cell membranes easily.

The primary natural source of nicotine is the tobacco plant, but nicotine is also found in some amount in related plants. Small amounts are in foods of the nightshade family, such as tomatoes and eggplants. Consumption of nicotine has not been limited to the use of plants in which it naturally occurs. In 1828, the German scientists Posselt and Reiman isolated nicotine from tobacco leaves, and since then it has been added to other products. For example, it is widely used as an insecticide in such products as Black Leaf 40, which contains 40 percent nicotine sulfate.

EFFECTS OF NICOTINE

The first pharmacological studies of nicotine were initiated in 1843 by Orfila. Nicotine is an alkaloid that affects major organs, such as the heart and brain. It also affects the body at the cellular level.

Effects in the Body. The actions of nicotine in a human body are complex. They depend on the amount of nicotine given, the route of administration (e.g., by mouth or intravenously), the time over which the dose is given, and the individual's history of exposure to nicotine. In high doses, nicotine produces nausea, vomiting, convulsions, muscle paralysis, cessation of breathing, coma, and circulatory collapse. Such high doses are seen after accidental absorption of a nicotine-containing insecticide or an overdose of nicotine.

In lower doses, such as those used by people who consume tobacco products, the effects are very different. They include a speed up in heart rate and blood pressure; increased force of contraction of the heart; constriction of blood vessels in the skin, producing cool, pale skin; constriction of blood vessels in the heart; relaxation of skeletal muscles; increased body metabolic rate; and the release of hormones such as epinephrine (adrenaline), norepinephrine, and cortisol into the bloodstream. Nicotine's effects on the brain are very complex because nicotine works in part by enhancing the release of chemicals that transmit information from one neuron to another (neurotransmitters) by brain cells. For example, nicotine enhances the release of dopamine, which may produce pleasure; norepinephrine, which may suppress appetite; acetylcholine, which produces arousal; serotonin, which may reduce anxiety; and beta endorphin, which may reduce pain. The development of addiction to nicotine in tobacco users is attributed in part to many of the effects of nicotine that people find desirable.

Effects of Nicotine in Cells. Nicotine binds (attaches) to receptors on cell membranes that normally bind a neurotransmitter called acetylcholine. Acetylcholine, like other neurotransmitters, is a chemical released by nerve endings in the body that binds to certain receptors on cells and activates them. The activated cells communicate messages to other nerves or produce specific actions on body organs. Nicotine activates only certain of the receptors that bind acetylcholine. These receptors are now called nicotinic cholinergic receptors. Using the selective action of nicotine on cholinergic receptors, scientists are able to observe their activity separately from muscarinic cholinergic receptors, receptors activated by a chemical called muscarine.

Nicotinic cholinergic receptors are located at the ganglia in the autonomic nervous system, where there are specialized areas for communications between nerves, in the adrenal gland, at the neuromuscular junctions, where nerves attach to and activate muscles, and in many parts of the brain.

The greatest number of nicotine cholinergic receptors in the brain are found in the hypothalamus, hippocampus, thalamus, midbrain, brain stem, and many parts of the cerebral cortex. Nicotine acts on sensory receptors, including those that mediate pain sensations. The effects of nicotine on these specific receptors have been an important tool in studying the effects of neurotransmitters on cell receptors and on the nervous system as a whole. In addition, these studies provide information about the widespread effects of nicotine introduced into the body during tobacco use.

DEVELOPMENT OF PHYSICAL DEPENDENCE ON NICOTINE

Nicotine is the chemical substance responsible for physical dependence on tobacco products. During the development of physical dependence on a drug such as nicotine, brain chemistry and function change. They return to normal in the presence of nicotine and come to depend on the drug for normal function.

The change that results in normal function in the presence of nicotine is called neuroadaptation or tolerance. When tolerance develops after a period of use of nicotine, or of any drug, the same dose produces less of an effect than previously. Tolerance develops to many of the effects of nicotine. It is well-known that people smoking their first cigarette often experience nausea and vomiting. However, after repeated exposure to cigarette smoke, these effects disappear. Their disappearance is the development of tolerance to the toxic effects of nicotine in the cigarette smoke. Tolerance also develops to the more desirable effects of nicotine such as pleasure and alertness.

The development of tolerance is associated with changes in the brain, such as an increased number of nicotinic cholinergic receptors found in the brains of smokers studied at autopsy. The changes in the brain correspond to a state in which the tolerant brain comes to depend on nicotine for normal functioning. This state is called physical dependence.

Physical dependence also means that abstinence or withdrawal symptoms occur when a person who has taken a drug on a regular basis stops taking it. Physical dependence on nicotine has been clearly demonstrated. Thus a person who stops using tobacco after his or her body has adapted to the presence of nicotine will experience withdrawal symptoms in the form of irritability, restlessness, drowsiness, difficulty concentrating, impaired job performance, anxiety, hunger, weight gain, sleep disturbances, slow down in heart rate, and a strong urge for nicotine. In general, withdrawal symptoms are opposite to the effects produced by nicotine when a person who is not tolerant uses it. Thus a person will start using tobacco primarily to experience the desired effects of nicotine, but once the addiction develops, use of tobacco may be chiefly to prevent the emergence of unpleasant withdrawal symptoms. Use of a drug to prevent withdrawal is common in people who are addicted to a drug.

ABSORPTION OF NICOTINE FROM TOBACCO

Nicotine, which is absorbed into the body when tobacco products are used, can be absorbed by different routes and at different rates. Some products deliver nicotine in smoke that is inhaled. In tobacco smoke, nicotine is present in droplets that also contain water and tar. These droplets are carried by gases that include carbon monoxide, hydrogen cyanide, and nitrogen oxides. Such suspended droplets carried by gas are called an aerosol. When the aerosol is inhaled, the droplets are deposited in the small airways of the lungs, from which nicotine is absorbed into the blood stream. After absorption through the lungs, blood containing nicotine moves into the heart and then into the arterial circulation, including the brain. Nicotine reaches the brain within 10 to 15 seconds after a puff on a cigarette. This rapid delivery of nicotine to the brain produces more intensive effects than following slower delivery and provides the close temporal link between smoking and the development of addiction.

Nicotine is absorbed into the body in other ways. It can be absorbed in the mouth even if not inhaled in pipe or cigar smoke. In addition, not all

tobacco products deliver nicotine through smoke. Chewing tobacco consists of shredded tobacco or plugs of tobacco that are enhanced with licorice and other flavorings. These products are periodically chewed, and the saliva generated is spat out, hence the term *spit tobacco*. Oral snuff is finely cut tobacco. A portion of oral snuff, called a pinch, is placed between the lip and the gum. Nicotine is absorbed from these forms of tobacco more slowly than from inhaled smoke, but the total amount absorbed is similar. Nasal snuff is finely powdered tobacco that is sniffed into the nose, where nicotine is rapidly absorbed.

DOSES OF NICOTINE TAKEN IN TOBACCO

The dose of nicotine absorbed from a cigarette is on average about 1 milligram (mg). The average user smokes about 25 cigarettes a day, an average nicotine intake of 20 to 30 mg daily. The average amount of nicotine absorbed from chewing tobacco or snuff per day is similar to that obtained from cigarettes. A person who smokes 25 cigarettes a day will absorb about 200 grams of nicotine in 20 years of smoking.

NICOTINE-CONTAINING MEDICATIONS

Nicotine is available as a medication, used to assist people in quitting smoking. These medications are meant to provide nicotine to smokers as a substitute for nicotine formerly consumed from tobacco use. Nicotine medications reduce withdrawal symptoms and increase the likelihood that the individual will quit tobacco use. Two forms of nicotine medication are currently available. Nicotine chewing gum (nicotine polacrilex, also known as Nicorette) consists of nicotine in a gum that slowly releases nicotine during chewing. Each gum is typically chewed for about 30 minutes. People chew up to 16 pieces per day when trying to quit smoking.

Nicotine patches are applied to the skin. They release nicotine slowly through the skin over 16 or 24 hours, depending on the patch used.

Both forms of nicotine-replacement medication deliver doses of nicotine equivalent to that taken in by the average tobacco user. Nicotine chewing gum delivers about 1 to 2 mg per piece. Nicotine patches deliver from 5 to 21 mg, depending on the patch and its strength.

ELIMINATION OF NICOTINE FROM THE BODY

Nicotine in the body is eliminated primarily by breakdown by the liver. The rate of breakdown is such that the level of nicotine in the blood falls about one-half after two hours. This rate is also known as a half-life of two hours. The primary breakdown product of nicotine is cotinine. Cotinine levels in the body are about 10 times higher than those of nicotine. The half-life of cotinine is 16 hours, and cotinine persists in the body for 4 days after a person stops smoking. Cotinine levels can be measured as an indicator of how much nicotine a person is taking in.

NICOTINE ADDICTION

Addiction to nicotine is well documented. The development and characteristics of nicotine addiction are described in detail in a report from the U.S. Surgeon General published in 1988. In this report, *The Health Consequences of Smoking: Nicotine Addiction*, the surgeon general presents criteria for nicotine addiction including the following:

1. Highly controlled or compulsive use. Smokers have great difficulty abstaining. Seventy percent of the 45 million smokers in the United States today report that they would like to quit and can not.
2. Psychoactive effects. Nicotine, as described earlier in this article, has pronounced effects on the brain.
3. Drug-reinforced behavior. Tobacco use is motivated by a desire for the effects of nicotine. People do not smoke cigarettes that do not contain nicotine. Very few people choose to smoke cigarettes that deliver very low doses of nicotine.

Other factors lead to the conclusion that nicotine is addictive:

1. It is used despite harmful effects. Most people know that smoking is harmful to their health and continue to smoke. Many people who have nicotine-related diseases are still unable to quit.
2. Relapse following abstinence. Most smokers can quit for a few days or even weeks (abstinence), but most of these smokers return to smoking within a month. Typically, it takes

four or five attempts before a smoker is successful at quitting permanently.

3. Recurrent drug cravings. Most smokers have an intense craving or urge to smoke when they have not smoked for some period of time.
4. Tolerance
5. Physical dependence
6. Pleasurable effects

The last three factors were described previously.

Smokers carefully regulate nicotine intake to maintain desired levels of nicotine in the body. Such careful regulation is further evidence that nicotine is addictive. Smokers keep the amount of nicotine obtained from cigarettes constant in two ways.

1. When people are given cigarettes that are labeled as low-yield (see tobacco history for detailed discussions of yields), they smoke more intensively to obtain the same dose of nicotine they were used to obtaining from the higher-yield cigarettes.
2. When they are forced to cut down on the number of cigarettes they smoke each day, they will take in more nicotine per cigarette. Thus when smoking is restricted, smokers tend to maintain the nicotine in their bodies at close to levels maintained during unrestricted nicotine intake.

BEHAVIORAL ASPECTS OF TOBACCO ADDICTION

People continue to smoke both because they enjoy the direct drug effects of nicotine and because use of nicotine becomes associated with other pleasures through learning—for instance, when the pleasurable effects of nicotine occur repeatedly in the presence of specific cues or events in the environment. Eventually, those cues and events become a signal to smoke. For example, people often smoke after meals, while drinking a cup of coffee or an alcoholic beverage, during a break from work, while talking on the phone, or while with friends who smoke. After smoking in these situations hundreds of times, the user may find that these situations themselves produce a powerful urge for a cigarette.

There are other learned pleasures that keep people smoking independent of the pharmacological effects of nicotine. Handling of smoking materials, and the taste, smell, or feel of tobacco smoke in the throat, all can become associated with the effects of nicotine and then become pleasurable in themselves. A person who tries to quit must learn to give up not only the pharmacological actions of nicotine but also the aspects of smoking that have become pleasurable through learning. Urges aroused after learning an association between aspects of the environment and the pleasures of smoking prompt relapses in many people who have already overcome withdrawal from nicotine and quit tobacco use.

Smokers report many other reasons for their habit. For example, many smokers, particularly women, smoke to maintain lower body weight. Others seem to use tobacco to control mood disturbances, such as depression or anxiety.

COMPARISON OF ADDICTION TO NICOTINE AND OTHER DRUGS

Nicotine addiction is similar to and as powerful as addiction to other drugs, such as heroin, alcohol, and cocaine. All these drugs have psychoactivity and produce pleasure. They increase the likelihood that people will spend time looking for them and engaging in rituals while taking them and that users will continue to take them in the face of risk to their well-being and health. The psychoactivity of nicotine is subtle and does not interfere with normal functioning in daily life. Thus nicotine's psychoactivity differs from that of heroin and cocaine, which produces more intense euphoria and may be disruptive to everyday functioning. Despite this difference, nicotine is addictive. A subtle psychoactive effect, especially when experienced with each puff of smoke, taken hundreds of times a day, exerts a powerful effect on behavior over time. The magnitude of effect becomes apparent when each puff of cigarette is considered as a dose of nicotine. A smoker who takes 8 puffs per cigarette and smokes 20 cigarettes per day is receiving up to 160 doses of nicotine per day. The dosing is equivalent to 58,400 doses a year, or 1,168,000 doses after 20 years of smoking.

When difficulty in quitting and relapse after attempting to quit are compared, it becomes apparent that nicotine is even more addictive than other drugs of abuse. Ninety percent of all people who smoke cigarettes are addicted and have difficulty quitting. In contrast, only about 10 percent

of people who drink alcohol at all have difficulty controlling use and would be classified as addicted. The percentage of occasional versus addicted users of heroin and cocaine is not known, but when multidrug users are asked about which drug they would have most difficulty giving up, the choice is most commonly nicotine (that is, cigarettes). Relapse rates among adults after cessation of alcohol, heroin, and tobacco use are similar.

NICOTINE ADDICTION IN YOUTH

Ninety percent of all tobacco users begin smoking before the age of 20. The earlier in life one starts smoking, the more likely he or she is to become a regular smoker and the more cigarettes he or she will smoke as an adult. The development of addiction in youth involves a series of steps including

- a trying stage
- experimentation
- regular smoking
- nicotine addiction

The typical interval between trying and addiction is 2 to 3 years.

Initially, young people smoke for social and psychological reasons. The motivations include the influence of parents and friends who are smokers, and the positive images of smoking perpetuated in television and movies and in advertisements in magazines, at music and sports events, and on billboards. Personal factors also play a role. Some include poor school performance, low self-esteem, poor self-image, sensation seeking, rebelliousness, failure to take seriously the adverse effects of tobacco use, and depression or anxiety. While early stages of smoking usually consist of occasional sessions with friends, tolerance develops and withdrawal symptoms are experienced between cigarettes as smoking becomes more frequent. Many youths report withdrawal symptoms and difficulty quitting. They consider themselves addicted to tobacco.

TREATMENT OF NICOTINE ADDICTION

Treatment of nicotine addiction is discussed in the articles entitled *Treatment: Tobacco*. The approach may be summarized as follows. Initial therapy usually does not include drugs. Smokers are encouraged to pick a day and just stop (go cold turkey). Some smokers participate in formal behavioral therapies, such as those available in smoking-cessation clinics. Those who are unable to stop on their own or with behavior therapies are more likely to be highly addicted to nicotine and are candidates for pharmacological (drug) therapy. The main drug therapies for smoking are nicotine-containing medications such as chewing gum or transdermal (skin) patches.

See also **Addiction: Concepts and Definitions; Adolescents and Drug Use; Reward Pathways and Drugs; Tobacco: Smokeless; Tolerance and Physical Dependence; Withdrawal: Nicotine (Tobacco).**

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NICOTINE DELIVERY SYSTEMS FOR SMOKING CESSATION.

The majority of people who smoke want to stop; however, many find this task difficult due to their dependence on nicotine. The most likely cause for relapse early in a quit attempt is the occurrence of tobacco or nicotine withdrawal symptoms such as urges to smoke (craving) and mood disturbances. Smokers intuitively know that the most effective way to relieve such symptoms is by smoking a cigarette (relapse), and so dependence is perpetuated.

Six different nicotine delivery systems are licensed for smoking cessation, usually referred to as nicotine replacement therapy (NRT). The rationale for using NRT is to provide a temporary supply of clean nicotine (i.e., without the disease-causing agents found in tobacco smoke) to help ease the severity of tobacco withdrawal symptoms. Tobacco withdrawal symptoms are generally worst in the first two to four weeks after stopping smoking, but smokers are advised to use NRT for at least eight to twelve weeks. Although NRT is not a magic bullet, it nearly doubles the likelihood of long-term abstinence, and no difference in efficacy is observed between products. Such an effect on abstinence is independent of the intensity of behavioral support provided.

NRT products typically provide less nicotine than the average smoker obtains from cigarettes, and nicotine plasma concentrations are usually half those achieved from smoking. These products also provide nicotine more slowly than cigarettes, with time to reach peak plasma concentration longer than that observed after cigarette smoking. These pharmacokinetic differences may partially explain why NRT does not reduce withdrawal symptoms as effectively as cigarettes.

Despite evidence for the effectiveness of NRT, some smokers are reluctant to use it. One such barrier is the incorrect belief that nicotine is the main component in tobacco smoke responsible for smoking-related disease. Other barriers include beliefs that NRT is ineffective or not required, having heard of other smokers who have successfully quit unaided. Some smokers have tried NRT in the past and found it unhelpful. Common reasons for this failure are unrealistic expectations of how NRT works, incorrect use, and discontinuing the use of the product too early in the recovery period.

PRODUCTS AVAILABLE AS OF 2008

Nicotine Chewing Gum. Nicotine chewing gum was the first NRT developed and licensed for smoking cessation. The nicotine within the gum resin is released when chewed and absorbed via the buccal mucosa (lining of the mouth). For optimal use, the gum is chewed until a hot peppery taste is experienced, and then the gum is placed in the side of the mouth to maximize buccal absorption of nicotine. This process, known as the chew-park-chew technique, is then repeated over some thirty minutes.

The gum is available in two strengths, containing two or four milligrams of nicotine. People who are highly dependent (e.g., smoke their first cigarette of the day within thirty minutes of waking) should use the higher strength formulation. Approximately half of the nicotine contained within the gum is absorbed.

Nicotine Transdermal Patch. The transdermal patch provides a simple and discreet method of delivering a continuous, controlled nicotine dose. Two types of patches are available (sixteen and twenty-four hour delivery systems) with equal efficacy, and no evidence favors either system. Smokers should generally start on the highest strength patches and use these for eight weeks. During the following four weeks lower dose patches are available for weaning, although weaning is not strictly required. High dose (e.g., 42mg/24 hour versus 21mg/24 hour standard dose) patch use shows a modest treatment benefit over standard dose. However, this treatment may be reserved for smokers with high severity of tobacco dependence. Skin irritation is the most common side effect, so users should be informed to rotate the site of application daily.

Nicotine Nasal Spray (NNS). Nicotine nasal spray delivers nicotine in a way that produces blood concentrations that most closely resemble those following smoking, with peak plasma concentration of nicotine reached in about five to ten minutes. Each dose (one spray in each nostril) provides one milligram of nicotine. Some studies have shown NNS to be particularly helpful in highly dependent smokers. Disadvantages of NNS are commonly reported adverse effects (burning sensation in the nose, runny nose, watering eyes, sneezing, and cough), which are often a barrier to further use. However, informing people of such effects and reassuring them that they will become tolerant to these effects in a short time may mitigate early discontinuation of treatment.

Nicotine Inhaler. The inhaler is a small plastic tube containing a replaceable nicotine cartridge. Nicotine vapour is released on puffing. Despite the product name nicotine is not inhaled into the

lungs but absorbed through the lining of the mouth. With ideal use (puffing on the inhaler for twenty minutes) up to two milligrams of nicotine can be absorbed, thereby reaching the amount of nicotine supplied by one cigarette. As with nicotine gum, lozenge, and sublingual tablets, a peak plasma nicotine concentration is reached within twenty to thirty minutes. The inhaler may be beneficial to people who miss the behavioral and sensory aspects of smoking.

Sublingual Tablets (Microtabs). These small tablets, containing two milligrams of nicotine, are designed to be placed under the tongue where they dissolve slowly over twenty to thirty minutes. Approximately half of the nicotine contained in these tablets is absorbed. This product is suitable for all smokers and one or two tablets can be used on an hourly basis. Advantages of this product are that it is small and discrete and is a good option for those that cannot chew gum (e.g., people with dentures, or poor dentition, commonly found in older smokers).

Lozenges. The lozenges are available in high and low strengths, which differ in nicotine content depending on the manufacturer (e.g., Novartis: 2 mg and 1 mg; GlaxoSmithKline: 4 mg and 2 mg). Like the nicotine gum the higher strengths are recommended for highly dependent smokers. Lozenges are generally easy to use.

With all oral NRT products (gum, sublingual tablet, lozenge, inhaler), nicotine is absorbed across the lining of the mouth. It is, therefore, important to ensure correct usage of these products to maximise nicotine delivery. Incorrect use of oral products, for example, chewing gum too vigorously, usually results in more nicotine being swallowed. Doing so is not hazardous but reduces the efficacy of the product because swallowed nicotine is not systemically absorbed (due to high first pass liver metabolism from nicotine absorbed from the gut) and increases the likelihood of adverse effects such as local irritation of the throat and esophagus from nicotine often results in heartburn or hiccups. Also common to oral NRT products is an initial unpleasant, irritating taste, which may be a barrier to correct use. Users of such products should be warned of this effect and assured that tolerance to this taste develops after a short period (usually a few days). While these products can be used on a regular (for example, hourly) basis, they may be used either more frequently and/or when urges to smoke are more intense.

COMBINING NRT PRODUCTS

NRT products can be safely combined and such use increases the odds of stopping smoking compared with using a single product. This advice contradicts some NRT product labelling that often states the contrary, that patients must use only one nicotine product at a time. Smokers should be informed of this contradiction when a clinician advocates combination therapy. A combination strategy usually combines a patch with a faster acting product for relief of breakthrough craving. The increase in effectiveness may be due to either higher nicotine levels or the additional sensory replacement achieved with the second product.

SAFETY OF NRT

Many smokers are concerned about the safety of using nicotine replacement products to quit smoking. Despite its addictive properties, nicotine has not been linked to the pathogenesis of respiratory disease, atherosclerosis, or carcinogenesis. Nicotine exposure increases heart rate and causes vasoconstriction of some blood vessels, which has led to concern when using NRT in patients with cardiovascular disease. However, controlled studies have demonstrated that, even in groups of smokers at high risk of cardiovascular disease, the use of NRT products does not increase the likelihood of acute coronary syndromes. NRT use in acutely ill patients has not been studied in detail; however, such treatment is a lesser hazard than continued smoking.

LONG-TERM USE

NRT is generally used for up to three months, although a small proportion of patients may need to continue to use it for longer. Of those who start NRT, 5 percent will generally continue to use it for up to a year. Patients who use NRT for longer are typically highly dependent smokers, so long-term NRT may be necessary to help them maintain long-term abstinence. Such long-term use has not been linked to any adverse outcomes.

Despite the strength of evidence supporting the use of NRT, it is not a panacea for smoking

cessation. At most, the long-term abstinence rates are about 20 percent. This outcome leaves people to wonder what makes the cigarette a better delivery system than currently available NRT products. The speed of nicotine delivery and total nicotine dose may be part of the answer; however, even nicotine given intravenously (simulating the rapid absorption achieved from a cigarette) does not completely remove urges to smoke. Research suggests that other, non-nicotine, components of tobacco smoke may have a role to play in reinforcing properties of smoking. These components include sensory and behavioral cues (e.g., the sensory effects of smoke in the mouth and throat and the action of puffing on a cigarette) and other chemicals that may increase the effect of nicotine on the mesolimbic dopaminergic pathway (the main pathway in the brain assumed to be responsible for dependence on tobacco and other addictive drugs).

New nicotine delivery systems are in development. Some aim to provide greater and faster nicotine delivery (e.g., NicoNovum oral pouch and mouth spray), whereas others are trying to combine nicotine with the sensory and behavioral components of smoking (e.g., Ruyan e-cigarette). Such products are hoped to provide greater withdrawal relief than products available as of 2008 and help more smokers to stop permanently. In the meantime, use of available NRTs should be encouraged and if used correctly will assist many smokers to achieve their goal of long-term abstinence.

See also **Tobacco: Dependence; Tobacco: Medical Complications; Tobacco: Smoking Cessation and Weight Gain.**

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NIGERIA.

BACKGROUND

With 140 million inhabitants (United Nations Development Programme [UNDP], 2007) Nigeria is by far the most populous country in Africa, accounting for one out of five people in the continent. The population is projected to grow to 176 million by 2015 and more than 300 million by 2050. About half of all Nigerians are under twenty-five years of age and the urban population more than doubled in thirty years, growing from 23 percent in 1975 to 48 percent in 2005. This relative youthfulness of the population and the rapid rate of urbanization (largely due to rural-to-urban migration) have major implications for psychoactive substance abuse in the country.

The use of licit and illicit drugs for a variety of social and psychological reasons is very much a feature of life in contemporary Nigeria. Alcohol is consumed more often than other drugs (especially in the non-Muslim regions of the country) but other substances—tobacco products, cannabis, amphetamine-type stimulants, cocaine, heroin, prescription drugs, and inhalants—are increasingly being used, especially among young people in urban areas.

Though there has been a relatively long tradition of research on the production, supply, and use of addictive substances, a lot remains to be known about the level of use of these substances in the general population and the consequences of their use on individuals, communities, and the society at large.

ALCOHOL

Although illicit drugs have focused the attention of policymakers and the public today, concerns about the role of alcohol in health and social problems in

Nigeria predate the country's independence in 1960 and were raised by both colonial administrators and local chiefs (Pan, 1965). Much of what is known today about drinking habits is based on surveys in the non-Muslim populations of central and southern Nigeria. There is agreement from several studies that at least 50 percent of adult males in Nigeria consume alcohol, with some surveys showing higher consumption rates (Ibanga, 2005; Gureje et al., 2007; Obot, 2007).

Many western commercial beverages are available in the country but beer is the most popular drink. Traditional homemade beverages (especially palm wine, fermented drinks, and distilled products) may account for more than 50 percent of the drinking by some people, particularly among those in rural areas and the impoverished in urban settings.

An analysis performed by the World Health Organization (WHO) of alcohol per capita consumption (APC) places Nigeria at the high end, with an adult APC of ten liters in 2001, the second highest in Africa after Uganda (WHO, 2004). What this figure means is that although a high proportion of Nigerians (especially women) do not drink at all, the drinkers among them consume large amounts of alcohol when they drink. Indeed drinking in Nigeria (as in many developing countries) is characterized by a pattern of heavy episodic consumption that is common to both male and female drinkers.

This habit of drinking to intoxication results in injuries and an overall high burden of disease. Although no separate analysis has yet been conducted for Nigeria, the country belongs in the group of African countries with the highest levels of estimated detrimental effects attributable to alcohol (deaths and years of life lost) especially among men (Roerecke et al., 2008). Hospital admissions data indicate that harmful drinking also seems to have significant effects on the mental health of Nigerians and has been implicated in road traffic accidents and violence.

TOBACCO

There has been a longstanding local production of tobacco products, especially cigarettes and snuff, in Nigeria dating back to about 1912 when the Nigerian Tobacco Company (NTC) was established. In 2000 the NTC merged with British American Tobacco (BAT) to form a company that today dominates a growing and unregulated cigarette market in Nigeria. The tobacco industry is supported by tens of thousands of local growers in the western and northern parts of the country and encouraged by favorable government policies.

Studies conducted in the 1970s and 1980s showed that more than 20 percent of adults were lifetime cigarette smokers (Obot, 1990). According to data compiled by WHO, 20 to 29 percent of boys and more than 10 percent of girls of high school age have smoked at least once. In a recent study by Oye Gureje et al. (2007) 17 percent of the adults (18 years and older) sampled randomly from across the country reported lifetime use of tobacco products and less than 4 percent were current users. Though findings from various studies are incomparable, what seems to be true is that a typical smoker in Nigeria smokes fewer cigarettes per year than a smoker in western countries, probably because of the cost involved.

Most Nigerian smokers are male but the use of snuff might be equally prevalent among adult males and females. Although there is little debate that tobacco use is associated with a wide array of health problems, few studies exist that link smoking with these problems in Nigeria. But there is bound to be more interest in smoking-related problems because of increased marketing and promotion activities by the tobacco industry.

CANNABIS

Among the illicit drugs used in Nigeria, cannabis has been around the longest, and public concerns about its abuse started soon after the country gained its independence. The use of the drug can be traced to the first generation of published papers on substance use (Asuni, 1964; Lambo, 1965). The plant, *Cannabis sativa*, was brought to the country by soldiers returning from the Second World War in North Africa and the Indian subcontinent (hence known locally as Indian hemp) in the 1940s (Asuni, 1964). Since then it has become highly domesticated, growing easily in the tropical and semitropical regions of the country and providing an avenue for illegal activities among many young people.

Cannabis has received overwhelming attention among illicit drugs partly because it has been around longer and also because of early studies linking its use to mental disorders. These studies showed that 8 to 20 percent of young people admitted into psychiatric hospitals had histories of cannabis use (e.g., Lambo, 1965). Later studies have confirmed the high prevalence of reported cannabis use among psychiatric inpatients and outpatients (Ohaeri & Odejide, 1993).

Studies among university students in the 1980s showed lifetime use of up to 8 percent, and 2 percent among secondary-school students. A recent general population survey of adults showed lifetime use of nearly 3 percent and less than 1 percent in the past year. Other studies in special populations, for example, school dropouts in urban areas, show much higher rates—as high as 10 percent in the past year and 8 percent in the past month (Obot et al., 2001). Like many other substances, including cocaine and heroin, cannabis seems to be a drug of choice of young people, especially those living in urban areas where access is much easier.

COCAINE, HEROIN, AND INJECTING DRUGS

It was not until the early 1980s that other illicit drugs began to make their mark in the country as commercial and consumer products. Although there had been anecdotal evidence of cocaine and heroin use during parties by "well placed Nigerians" and "expatriate workers" in the early 1980s (Ebie & Pela, 1981), it was not until the first arrest of a trafficker in 1982 that the two drugs became known by the Nigerian public (Obot, 2004). Since then and following what at times has been a significant role of Nigerians in the international drug trade (serving mostly as traffickers between producing and consuming countries), cocaine and heroin have entered into the national discourse on security issues, international relations, and criminal justice.

Like cannabis, information gathered from psychiatric hospital clients provided the warning signs that young Nigerians were not only involved in trafficking these drugs but also using them. In nontreatment samples almost all available studies show that approximately 1 percent of young people surveyed have used one or more of these drugs at least once, usually in their smokable forms or by inhalation (*chasing the dragon*).

Information regarding the use of drugs via injection is known today largely based on three studies funded by the World Health Organization and the United Nations Office on Drugs and Crime (UNODC) (Adelekan & Lawal, 2006). Twenty-one percent of more than 1,000 drug users interviewed had injected heroin, cocaine, or some other drug at least once, and 8 percent were current injectors. The studies did not show that drug injectors were more likely than non-injectors to be infected with HIV.

NONPRESCRIPTION USE OF SEDATIVES AND STIMULANTS

While there has been greater regulation of the manufacture, prescription, and sale of pharmaceutical products in recent years, limited availability and poor accessibility of professional health-care services have forced many to self-medicate with over-the-counter and prescription drugs, some of which have high abuse potentials. Many of the drugs used without prescription are tranquillo-sedatives (sleeping aids) and opioids or analgesics (to suppress pain). The abuse of pethidine (meperidine) by physicians and nurses was reported in the early 1980s and valium and codeine remain popular drugs of abuse.

In a recent general population survey of about 7,000 adults, 16 percent of males and 12 percent of the females interviewed reported lifetime nonprescription use of sedatives (Gureje et al., 2007). Unlike the use of other substances initiated in early adolescence, this study showed that prescription drug use started between twenty and forty years of age.

The use of drugs that stimulate the central nervous system is an old practice in Nigeria. One of the most culturally accepted addictive substances is the kola nut, the dried cotyledon of the local tree *Cola acuminata*, grown mostly in the south but chewed by adults across the country. The use of modern stimulants (known in different regions as *brain pills* or *sleepless pills*) was identified in the 1970s as a problem among young people who took dexamphetamines (Dexedrine) and Pro Plus (a preparation containing 50 milligrams of caffeine per tablet) as study aids (Oviasu, 1976). Other psychostimulants like pemoline, ACD (alleged to be a mixture of aspirin, codeine, and dexamphetamine), and native herbal preparations are also used

by workers, long-haul drivers and students for increased energy and to stay awake (Ohaeri & Odejide, 1993). Like cannabis, stimulants were associated with mental illness among young users, especially males (Oviasu, 1976). A mental condition identified in Nigeria in 1960 and known as *brain fag syndrome* was suspected to be associated with the abuse of these drugs by students who sought relief from the mental fatigue that developed from studying for exams.

RESPONSE TO DRUG PROBLEMS

Laws against illicit drugs were enacted after Nigeria's independence, beginning with the Indian Hemp Decree of 1966 to the omnibus National Drug Law Enforcement Decree of 1989, and remain the basis of legislations. Stringent punishment for possession and use of cannabis, cocaine, and heroin has been at the center of these legislations (Obot, 1992). Nigeria is a signatory to all UN conventions on drug control and has also ratified the Framework Convention on Tobacco Control (FCTC), but it currently lacks a policy framework for controlling the sale of and harmful consumption of alcohol.

Demand for the treatment of drug and alcohol problems has been growing for many years but opportunities are still grossly limited. Although nonprofit organizations and religious groups are increasingly involved in the provision of services, most available treatment slots are still in psychiatric hospitals and only some of these have dedicated units.

Like other developing countries, Nigeria is struggling with many seemingly unyielding social problems and little attention is paid to substance use and dependence except for declarations of war against illicit drugs and sporadic activities on demand control—prevention of use and treatment of dependent individuals. However, like smoking, illicit drug use and harmful consumption of alcohol increases among Nigeria's growing population of young adults in urban settings. The country will have to come to terms with the health and social burden that substance abuse imposes on the society and seek effective ways to confront the problem.

See also **Africa; Foreign Policy and Drugs, United States; International Drug Supply Systems; Kenya; South Africa.**

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ISIDORE OBOT

NMDA (N-METHYL D-ASPARTIC ACID). *See* **Receptor: NMDA (N-Methyl D-Aspartic Acid).**

NORDIC COUNTRIES (DENMARK, FINLAND, ICELAND, NORWAY, AND SWEDEN). This article deals with alcohol, tobacco, and drugs in the Nordic countries situated at the northwest corner of Europe: Denmark, Finland, Iceland, Norway, and Sweden. Denmark is the southernmost of the Nordic countries; it has a land border with Germany in the south and is separated in the north from Norway by the Skagerrak strait and from Sweden by the Kattegat and Öresund straits. Since 2000 a bridge has also connected Denmark with Sweden. Norway lies farthest west on the Scandinavian Peninsula, separated mainly by mountains from Sweden that occupy the eastern side of the peninsula. Finland lies east of Sweden and has a land border with both Norway and Sweden in the north; in the west it is separated from Sweden by the Gulf of Bothnia. In the south the Gulf of Finland separates Finland from Estonia and in the east Finland has a nearly 1,300 kilometer land border with Russia. Iceland lies in the Atlantic Ocean about 1,000 kilometers west of Norway.

The history of Denmark goes back to the beginning of the Viking age, from approximately 800 to 1050. In 1397 the Kalmar Union brought together the thrones of Denmark, Norway, and Sweden under Queen Margrethe I of Denmark. Finland became a part of Sweden in the twelfth century. Sweden broke from the Kalmar Union in 1523 and developed into a powerful European nation. Norway remained in the union until 1814 when it was given to Sweden as a consequence of the Napoleonic wars. In 1809 Sweden lost Finland to Russia. Finland became independent in 1917. In 1905 Norway peacefully separated from Sweden. Iceland, populated in the late ninth century, belonged to Denmark from 1262 to 1944 when it became independent.

The Nordic countries are quite homogenous with regard to population and language. Finland is an exception insofar as Finnish belongs to the Finno-Ugric language family, whereas the languages spoken in the other Nordic countries are considered Germanic. In all Nordic nations the principal church is Evangelical Lutheran, although many belong to the church only in name. As of 2008, a clear majority of the population lives in cities and towns, and about two-thirds of those employed work in the service sector. Less than 5 percent earn their livelihood from agriculture. In the Nordic countries, as in all industrialized European nations, this is the outcome of a pronounced migration of people from the countryside to towns and larger cities and from agriculture to industries and services. In 2006 the gross domestic product per capita was about 30,000 euros in the Nordic countries, with the exception of Norway where it was 42,000 euros. The Nordic nations are famous for their welfare state system. Welfare schemes are universal and they guarantee social and economic security and welfare services, which include health care, unemployment benefits, and education.

This entry will first give a brief historical overview of the appearance of alcoholic beverages, tobacco products, and other drugs in the Nordic countries. It will then examine the consumption and control of alcohol from about 1850, when home distilling was prohibited and the downward trend in alcohol consumption began. This is followed by an analysis of smoking and its control, from the late nineteenth through twentieth centuries, when mass-produced cigarettes became the most important way to smoke and consume tobacco. Illegal drugs are treated in a similar manner, starting with developments in the 1960s when recreational drug use began to spread to the Nordic countries. Differences in the regulation of alcoholic beverages, tobacco, and drugs will be addressed in the concluding section.

APPEARANCE OF ALCOHOLIC BEVERAGES, TOBACCO, AND DRUGS IN THE NORDIC COUNTRIES

During the Viking age, beer was the dominant alcoholic beverage in Nordic countries. At that

time beer was also an important beverage with meals and it was commonly consumed. The quality and alcohol content of Viking age beer were, however, lower than those of beer brewed in this century. Mead was also a popular alcoholic beverage, but it was later replaced by imported wine.

Wine is not produced in the Nordic countries, but the Vikings did become familiar with it during their journeys to the British Isles, Mediterranean countries, and Russia. As an imported product, wine was quite expensive and, therefore, its regular consumption did not spread among the common people. Like beer from the same period, the wine of the Middle Ages had low alcohol content, and transporting wine from central Europe to the Nordic countries only further worsened its quality. As a result, honey and spices were frequently added to wine to make it drinkable.

Beer continued to be the dominant alcoholic beverage in the Nordic countries until the eighteenth century. In the late seventeenth century distilled spirits first became known in the Nordic countries as a medicine. However, they quite rapidly transformed into a widely used intoxicant, soon replacing beer as the dominant alcoholic beverage. According to some estimates, the per capita consumption of distilled spirits in Sweden in the first half of the nineteenth century was about 40 liters or nearly 20 liters converted to 100 percent alcohol. At that time, the consumption of distilled spirits was also very high in other Nordic countries.

Smoked and smokeless tobacco became known in Europe in the late sixteenth century after Europeans had encountered and traded with Native Americans. The use of tobacco spread very quickly in Europe and reached the Nordic countries at the beginning of the seventeenth century. At that time, the most common tobacco products were chewing tobacco and powder tobacco for nasal inhalation. Moist snuff is another form of smokeless tobacco that became very popular in Sweden in the late eighteenth century when the habit of smoking was still uncommon, given the expense of producing cigars, cigarettes, and pipes. Smoking tobacco also needed a safe and ready source of fire. In the nineteenth century, however, pipe smoking became increasingly popular in the Nordic countries and paved the way for a great increase in smoking, one connected with the mass production of cigarettes and the development of safety matches later that same century.

Opium, morphine, and heroin arrived on the Nordic scene solely in the form of medicines at the end of the nineteenth century. Regarded as poisons and strong medications, they were soon placed under the control of pharmacies and the medical profession. In the Nordic countries the misuse of these medicines seems to have been limited to a few persons, primarily those who had easiest access to them, such as doctors and nurses. Morphine and heroin were used more extensively as cough medicines and painkillers in wartime. It was estimated in 1946, for instance, that during World War II some 100 to 200 former soldiers in Finland had become addicted to heroin. Otherwise, the framework for a control policy in this area may be said to have developed in international organizations such as the League of Nations and later the United Nations, in which international conventions aiming to control and criminalize the production, trade, and use of drugs for other than medical purposes were designed. When the Nordic countries became parties to these conventions, the abuse of drugs including cannabis was largely unknown in that part of the world.

USE AND CONTROL OF ALCOHOLIC BEVERAGES

In the eighteenth century the distilling of spirits was already controlled in the Nordic countries, not so much because of the adverse effects of drinking on public health or social order, but because distilling spirits competed with another important use of grain, namely to feed people and especially soldiers. At the beginning of the nineteenth century, restrictions on home distilling weakened, and along with the increase in drinking and peacetime after the Napoleonic wars, the consumption of distilled spirits came to be regarded more and more as a question of social order.

The mid-nineteenth century saw the birth of the temperance movement in the Nordic countries, with nationwide total prohibition as its ultimate goal. At that time, the Nordic countries also needed more and more tax revenue for several important purposes, such as building railways and other modern infrastructure. These two factors together resulted in the banning of home distilling

in the Nordic countries in the mid-nineteenth century, with the purpose of moving the distilling of spirits into more controllable licensed distilleries.

In the second half of the nineteenth century the attempts to control the adverse social effects of drinking led to more stringent alcohol control measures. In Finland, for example, this meant that by World War I alcoholic beverages, with the exception of beer, were no longer available in the countryside. In towns, the Gothenburg system, designed to reduce private profit motives and to derive public revenues from the sale of alcoholic beverages as well as to control alcohol-related social problems, was spreading very quickly. The Gothenburg system had originated in the Swedish mining town of Falun in the 1850s. Starting in 1870, locally authorized liquor stores had also been established in Norway. As a direct result of these policy measures, distilled spirits and total alcohol consumption continued to decrease in all Nordic countries until World War I, which became a turning point in Nordic developments concerning alcohol.

In 1917 Denmark, because of the shortage of foodstuff, increased the tax on distilled spirits 12-fold and the tax on beer by 60 percent. This led to a dramatic decrease in spirits consumption, and in one year the share of beer in total alcohol consumption increased from 30 to 83 percent. At that time, wine's share of total Danish alcohol consumption was about 5 percent. The tax increase was followed by a decrease in alcohol-related problems and also the Danish temperance movement lost its rather strong foothold. Consequently, Denmark never established any prohibition acts or state alcohol monopolies, and public attitudes toward the drinking of alcoholic beverages focused, until the early twenty-first century, almost exclusively on the need for individual self-control and responsibility.

In Sweden in 1917, the Gothenburg system evolved into a system whereby local monopolies were granted exclusive rights to the sale of wine and distilled spirits. In addition, a monopoly on the production, import, and wholesale distribution of distilled spirits was established. After a referendum in 1922, in which the temperance movement lost, a unique system known as the Bratt system was introduced in Sweden. This system was based on the use of a ration book that was forwarded to those citizens assumed to drink distilled spirits without causing social damage. Generally, ration books were issued only to men because married women were expected to share their husband's allocation. Unmarried women and young males had smaller monthly rations than adult men, whose share as a rule was set at 4 liters of distilled spirits per month. The minimum age for receiving a ration book was 25 years. The ration book permitted alcohol purchases in only one monopoly shop; all purchases were recorded in it and government authorities could also seize the book if they noted that circumstances warranted such. The Bratt system was eliminated in 1955 at the same time as a law came into effect permitting the sale of beer with greater alcohol content in Sweden.

Iceland introduced prohibition in 1915. In Finland and Norway, the shortage of food during World War I led to a nearly complete prohibition of alcoholic beverages. In Finland, a prohibition act was passed by a unanimous vote in parliament in 1907 but only became effective in 1919; it banned all beverages containing more than 2 percent ethyl alcohol by volume. Norway instituted a prohibition of distilled spirits and fortified wines after a nationwide referendum in 1919. The prohibition on fortified wines was revoked in 1923 and that on distilled spirits in 1927. In Finland, prohibition was repealed in 1932. In Iceland, prohibition lasted until 1922 with regard to wine and until 1935 with regard to distilled spirits; beer was prohibited until 1989.

After prohibition ended, Finland, Iceland, and Norway introduced an alcohol control system based on a comprehensive state alcohol monopoly, the restricted physical availability of alcoholic beverages, and high alcohol excise duties and prices. After the Bratt system, Sweden also adopted a similar kind of alcohol control system but with two separate monopolies: one for the off-premise retail sale of alcoholic beverages and one for their production, import, export, and wholesale distribution.

Nordic control systems have differed on how beer sales are controlled. In Norway, beer with greater alcohol content was sold in ordinary grocery stores until 1993, after which it has only been sold in the alcohol monopoly's outlets. In Finland, all beers were sold only in monopoly liquor stores

until 1968, after which beer with a maximum alcohol content of 4.7 percent by volume has been sold in ordinary grocery stores. In Sweden, beer with a medium amount of alcohol was sold in groceries from 1965 to 1977, after which all beers over 3.5 percent alcohol by volume have been sold only in monopoly liquor stores.

During the period between World War I and II, Sweden experienced the highest alcohol consumption in the Nordic countries, about 3 liters per capita a year. In Finland, annual per capita alcohol consumption was just a little over 1 liter, the lowest figure among the Nordic countries at that time. Between the world wars, distilled spirits was still the most preferred alcoholic beverage category in the Nordic countries, with the exception of Denmark.

After World War II, alcohol consumption grew in the Nordic countries as in all Western industrialized nations until the mid-1970s. At that time, recorded annual alcohol consumption in Denmark reached 10 liters per capita. In Finland and Sweden, the corresponding figure was 6 liters, and in Norway and Iceland, about 4 liters. Besides economic growth, an increase in leisure time, migration, and other significant changes in living conditions as well as the increase in alcohol availability contributed to this growth. The number of retail outlets also increased, as did their hours of operation. Many regulations making the consumption of alcoholic beverages quite difficult in restaurants have been lifted and age limits for the purchase of alcoholic beverages have been lowered.

Since the mid-1970s recorded alcohol consumption in Denmark has decreased to 9 liters per capita a year. In Finland, it has increased to nearly 9 liters. If unrecorded alcohol use is added to the recorded statistics, total annual alcohol consumption in Denmark and Finland is approximately 10.5 liters, the same as in France and higher than in Italy. In 2006, annual recorded alcohol consumption was just over 5 liters in Iceland, Norway, and Sweden. When unrecorded alcohol consumption is added, total annual alcohol consumption in Sweden was 8 liters and in both Iceland and Norway about 6 liters per capita.

During the last three decades of the twentieth century the consumption of distilled spirits decreased and wine consumption increased in all Nordic countries. Beer consumption decreased in Denmark, stayed about the same in Sweden, and increased in Finland, Iceland, and Norway. These developments meant that as of 2008, the most preferred alcoholic beverage in all Nordic countries was beer, followed closely by wine in Denmark and Sweden.

Until the 1990s, changes in alcohol availability were mostly of domestic origin. After Finland and Sweden joined the European Union (EU) in 1995, and Iceland and Norway decided to participate in the European Economic Area agreement in 1994, mostly international developments molded the Nordic alcohol control system. In practice, this meant that the Nordic monopoly countries have lost their monopolies on the production, import, export, and wholesale distribution of alcoholic beverages.

European economic integration has also affected alcohol taxes as the creation of a single European market eliminated travelers' alcohol import quotas. This put pressure on the Nordic countries through border trade, as their neighboring EU countries had significantly lower alcohol excise duties and prices. Denmark, an EU member from 1973, decreased its taxes on beer and wine by 50 percent in the early 1990s, and in 2003 decreased its taxes on distilled spirits by 45 percent. After its neighbor Estonia became a member of the EU, Finland was forced to decrease its alcohol taxes by 33 percent on average. Likewise, Sweden and Norway felt the pressure to reduce their high alcohol taxes although they decreased them to a lesser extent than Denmark and Finland. As an island, Iceland has been able to maintain its excise duties on alcohol, which remain the highest in Europe.

Increased economic integration has led to further increases in alcohol consumption in the Nordic countries since the mid-1990s with the exception of older EU-member Denmark. Especially in Finland and Sweden, travelers' alcohol imports rose to a new high in the beginning of the twenty-first century. Furthermore, the possibilities for making private profits in the alcohol industry have increased and led to harsher competition in alcohol markets with increasing marketing and advertising of alcoholic beverages.

In the early twenty-first century alcoholic beverages are commonly used in the Nordic countries,

with only 5 to 15 percent of the population reportedly abstaining from alcohol during the last 12 months. Among youngsters alcohol consumption is becoming more frequent from the age of 14 to 16, and at the age of 18 the rate of abstainers is almost the same as that among adults. No clear differences exist between the drinking habits of young adult males and those of females. Alcoholic beverages are most commonly used during leisure time involving recreational activities. In the Nordic countries, alcoholic beverages are not used regularly as beverages with meals, but it is quite common for those drinking to become intoxicated.

USE AND CONTROL OF TOBACCO

As long as tobacco use has existed in the Nordic countries, there have been constant debates about its influences and consequences, and both arguments of approval and disapproval have been voiced. For instance, in Sweden in the early twentieth century lively public debates ensued on both the negative health consequences of tobacco and on the moral character of young men in particular. Such concern, however, was confined to smaller societal circles until the 1950s.

Cigarette smoking became increasingly common and socially accepted during the twentieth century. One could say that smoking was the norm embedded in most social contexts. During wartime a ration of cigarettes was seen as every soldier's right and the tobacco industry boomed. Later, there were compartments for smokers in buses, trains, and airplanes and few restrictions on smoking in public places. At good dinners the host's offer of a cigarette was customary. Sporting activities and tobacco were seen as an acceptable combination, and up until the 1960s and 1970s cigarettes figured freely in advertisements, news clips, television programs, and movies. Smoking was seen, however, as an adult preoccupation, and thus in Norway, for instance, the municipalities could restrict selling tobacco to youngsters under the age of 15, and after 1935, the law forbade pupils and students to smoke in the nearby surroundings of their schools. In the 1970s in Finland, in contrast, ashtrays, which older pupils used during breaks, were often observed in schoolyards.

In the majority of the Nordic countries the generations born between 1910 and the end of the 1930s, especially men, were the most frequent smokers. At the end of the 1940s around 75 percent of all Finnish men in the 20 to 40 age group and in Norway 80 percent of all men 20 to 24 years old were smokers. Even if it was customary to smoke tobacco in pipes, cigarette smoking became the dominant mode during World War II. Interestingly enough, homemade cigarettes were the most frequently used form of tobacco in Norway in 1960. Also in Sweden, 50 percent of all men and 9 percent of all women were regular smokers in 1946, the smoking habit being, however, even more prevalent among younger age groups. Sweden was a clear exception to the smoking habit: In the 1840s moist snuff, called *snus*, became the most popular tobacco product among men, but in the period after World War II until 1970 the sales as well as the use of snus declined.

In the 1950s, and especially in the 1960s, medical evidence on the disastrous health effects of tobacco smoking, especially its relation to lung cancer, spread throughout the world. The effects on consumption were soon seen all over Europe, and smoking rates have declined in the decades since. In the early 1970s, 51 percent of adult Norwegian men smoked daily compared to 32 percent of women. In 2007 these figures were 21 and 23 percent, respectively. Similar statistics apply to the other Nordic countries: Between 2002 and 2005 the overall rates of daily smokers in the entire population averaged between 16 and 25 percent, rates that from a European perspective are at the lower end. The lowest percentage may be attributed to Sweden, given the persistent use of snus. In 2006 only 12 percent of Swedish men and 17 percent of women were daily smokers. The fact that more women than men are regular smokers is internationally unique. The use of snus has, on the other hand, increased during the last 15 years. As of 2008, Sweden is the only EU country in which trade with snus is allowed. Snus usage is a distinct male habit making up for the comparatively low levels of smoking among Swedish men. In the late 1980s 17 percent of Swedish men were regular snus users, increasing to 23 percent by 2005. The corresponding figures for women were 1 percent and 3 percent. The European Economic Area Agreement also allows for snus in Norway but the snus market there has remained small.

Measures to reduce smoking and the consumption of tobacco products in general have been

taken up in all the Nordic countries since the 1960s, and they have with small variations followed the same path. On the whole, Denmark is the nation that seems the least restrictive and was also the last to introduce new restrictions. Thus, for instance, both Norway and Finland banned tobacco advertisements and sponsorship in the 1970s as well as the use of tobacco brand-names for other products in 1997. Health warnings on tobacco products were also instituted. In Denmark only, ads on radio and television, and youth-directed advertising, were not prohibited until the end of the 1980s, and it was not until 2001 that Denmark also forbade the use of cigarette names on other products. In the 1970s the Nordic countries also explicitly outlawed the sale of tobacco to young people, the age limit often being 16, as was mandated in Norway in 1975 and in Finland in 1977. In these nations, as well as in Sweden the age limit was raised to 18 in the mid-1990s, whereas Denmark introduced the age limit of 16 in 2004.

In the 1980s and 1990s, again on the basis of increasing evidence of the negative effects of so-called second-hand, or passive, smoking, the focus in tobacco control shifted to the protection of third parties. First in line were restrictions on smoking in public places, and in connection with that the protection of the workforce in workplaces in general and in restaurants in particular. As of 2008, all Nordic countries have either completely prohibited or severely restricted smoking in restaurants or cafés. In the early twenty-first century tobacco control developed within the EU system with directives and regulations in several key areas: public health policy, taxation, workplace environment, and agricultural policy.

USE OF OTHER DRUGS AND DRUG CONTROL

In contrast to drinking, drug use has never been regarded as a socially or culturally acceptable behavior in the Nordic countries. Ever since the early beginnings of recreational drug use in the 1960s it was recognized as a serious social problem. It thus has attracted much public interest and attention.

Drug use spread to the Nordic countries in the 1960s and 1970s in connection with the student and youth movements, "flower power," and alternative lifestyle ideologies. The fact that drug use was mostly confined to these cultural settings meant that it was mainly an urban phenomenon among upper- or middle-class youth as well as segments of the cultural elites. By the time the use of drugs spilled over from better-off young people to "not so well to do" youth, the assortment of available drugs, which originally included cannabis and psychedelic drugs such as LSD, also incorporated amphetamines and opiates. In addition to experimental or recreational drug use, which mostly consisted of pot smoking, more problematic consumption and abuse emerged.

In Denmark and Norway, the intravenous use of opiates dominated heavy drug use, whereas intravenous amphetamine use dominated problematic drug use in Sweden. Both experimental and problem use was much more prevalent in Denmark than in any other Nordic country, with Finland and Iceland recording the least use, and Norway and Sweden somewhere in between. However, during this same time period the vast majority of youth and adults in all Nordic countries had no personal experiences with illegal drugs.

The initial appearance of drugs in the Nordic countries was countered by reformulations of existing criminal laws and specific new national drug laws. A range of behaviors, especially those tied to selling or marketing drugs, were criminalized and harsh penalties mandated. Societal measures also included the establishment of youth clinics and therapeutic communities for young abusers, and the compulsory treatment of young, mostly underaged, users.

Until the 1980s drug policy was a kind of residual system: It had few features of its own but worked mostly on the basis of more general criminal, welfare, and health policies. Increasing international cooperation on drug policy emerged with the Western War on Drugs ideology, but Nordic drug policy also became more distinct in its own right, even if the responses to the drug problem differed somewhat between countries. One common feature was the emphasis on a balanced approach to contain the drug problem: prevention, treatment, and control. In Denmark, legislation made a distinction between soft drugs (mostly cannabis) and hard drugs, and Denmark also embraced early on an approach more oriented toward harm

reduction. Sweden and to some degree Norway aimed at a drug-free society and pursued a rigorous policy toward achieving this goal.

In the 1990s new recreational lifestyles brought with them new drugs, such as Ecstasy and other party mixtures, and their use spread among youth in the Nordic countries. Compared to the 1960s, this second drug wave was more pervasive as it took place in a new media- and information-oriented society, with an emphasis on consumption, risk-taking behaviors, and individualism. The growth of drug use in the Nordic countries was also facilitated by easier access to and the lower costs of drugs, due partly to the new drugs arriving from Eastern Europe. The increase in drug use was most obvious in Nordic countries other than Denmark, but still by the mid-1990s only about 1 out of every 3 adults in Denmark, and 1 out of every 10 adults in other Nordic countries, had any experience with drugs.

The growth in the experimental use of drugs plateaued in the late 1990s, even reversing itself in the early twenty-first century. Data from the European School Survey Project on Alcohol and Other Drugs (ESPAD) on drug use among 15- and 16-year-olds show that in 2003 some 20 to 25 percent of Danish youth had used cannabis, whereas the corresponding figure in Iceland was approximately 15 percent and about 10 percent in each of the three remaining Nordic countries. The experimental use of drugs other than cannabis among 15- and 16-year-olds was much lower, between 1 and 4 percent.

Even if the trends in heavy drug use among the Nordic countries are difficult to discern, some characteristics stand out. The latest data indicate that the situation in Denmark is stable. In 2006 around 27,000 persons out of the Danish population of 5.4 million were estimated to be problematic drug users; of these, 7,000 used mainly cannabis. In Finland, whose total population is 5.3 million, the estimates are based on administrative statistics that revealed approximately 14,000 to 19,000 individuals used either amphetamines or opiates. In Norway, with 4.6 million inhabitants, the estimate of intravenous drug users is around 8,000 to 12,000, with most of them reporting opiates as their main drug. In Sweden, with 9 million inhabitants, the estimates on heavy drug users in 2004 placed that number at approximately 26,000, or the same as in 1998. The above figures are crude estimates based on different kinds of data and methods and are not directly comparable. Clinical data show that in Denmark and Norway heroin is still the most frequently used drug among problem drug users, whereas in Sweden, which previously reported the widespread use of injected amphetamines, opiates are used almost as frequently as amphetamines. In Finland, as of 2008, nonprescribed buprenorphine was above amphetamine as the most popular drug among heavy drug abusers. Iceland has also reported some heavy use of amphetamines and prescription medicines containing opioids.

It is a well-known fact that drug use may have various adverse health effects and cause premature death. Infectious diseases are more widespread among problem drug users, and their death rate is significantly higher than in the general population. In the Nordic countries, the overall level of HIV infections and proportion of individuals infected by intravenous drug use have remained low. Finland experienced a minor epidemic when injecting drug use increased rapidly in the late 1990s and the proportion of such users in the HIV-infected population reached 60 percent. By the early twenty-first century that situation had stabilized, thanks to the introduction of needle-exchange programs and other special services for drug users. The growing incidence of hepatitis, especially Hepatitis C, has also raised concern among Nordic drug users. Drug-related deaths are also more common in Denmark and Norway—around 4 to 5 per every 100,000 deaths—than in the other Nordic countries.

Drug policy in the Nordic countries still rests on three main principles: control of supply and counteracting criminality; prevention of use and misuse; and treatment and harm reduction. In the early twenty-first century there seems to be a move toward an increased focus on substitution treatment or medicalization, even in those countries that traditionally maintained a restrictive drug policy. Substitution treatment is in some form part of the treatment offered to drug users in all Nordic countries. Even Sweden, which has taken the most restrictive stance on medically assisted treatment, introduced substitution treatment with buprenorphine in 1999. As well as running treatment services, measures are

employed that seek to reduce drug-related harm in the group of drug users for whom a drug-free life seems unrealistic in either the short or long term. Harm reduction measures include such activities as outreach street work, low-threshold services at drop-in centers, low-threshold health-care centers, and syringe-exchange programs in most of the Nordic countries.

The major changes in the political structure of Eastern Europe and transformation of the former Soviet Union into Russia, however, also had consequences for the drug markets and drug supply in the Nordic countries. The most significant result has been—according to some observers—the increasing independence and size of the northern European illegal drug market, which formerly was an integral part of the broader European market. This has put pressure on the control side of drug policy.

Thus, even if substitution treatment and harm reduction measures have gained ground as responses to drug problems in the Nordic countries, there are no signs of downgrading the control measures. In Finland, for instance, policy has moved forward on a dual track of both increased control and increased harm-reducing measures. In the early twenty-first century Danish drug laws also became more restrictive while at the same time attempting to uphold the strong tradition of substitution treatment and harm reduction. Systems for substitution treatment and harm reduction developed notably in Norway since the late 1990s, with a new emphasis on the exchange of syringes and needles, experimental supervised injection rooms, and substitution treatment as well as specialized medical care.

ASSESSMENT

Consumption and policy regarding alcohol, tobacco, and illegal drugs exhibit both converging and diverging trends in the Nordic countries. On an individual level, drinking alcohol and smoking tobacco seem to be related activities, which the fears of restaurant owners on losing customers, as the result of bans on smoking in restaurants, bear witness to. Alcohol and other drugs are often seen by the greater public as substitutes for each other, but the concomitant use of alcohol and illegal drugs is, in fact, frequently the norm among drug users. On a broader level in terms of the general population, trends in alcohol and tobacco consumption do not coincide, as the use of alcohol has either increased or remained stable during the last several decades, whereas smoking has clearly diminished. Consumption trends in alcohol and other drugs are neither headed in the same direction nor going the opposite way.

In the early twenty-first century drinking alcohol is both legal and socially accepted in the Nordic countries, and traditional Nordic alcohol control has become weaker as more weight has been put on the individual's responsibility. European and global economic integration will in the future place even more weight on measures that affect the demand side of the alcohol equation and probably lead to further weakening of measures affecting the supply of alcoholic beverages as well as alcohol taxes and prices in the Nordic countries. Other drugs remain illegal and drug policy is somewhat restrictive, but that approach has been complemented with substitution treatment and harm reduction. The variations in drug policy among the Nordic countries seem to be smaller than was the case in the 1950s and 1960s. Smoking has become increasingly socially unacceptable and more heavily controlled with limits on advertising, establishment of age limits, and prohibition of smoking in public spaces, workplaces, and restaurants. These kinds of developments will no doubt continue as strict tobacco control also has become the norm on an international level, as exemplified in the Framework Convention on Tobacco negotiated under the auspices of the World Health Organization.

See also **European Union; Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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NOREPINEPHRINE. Also referred to as adrenaline, it is a catecholamine neurotransmitter known to be involved in the action of some addicting drugs. It is the biochemical product of dopamine and the enzyme dopamine-beta-hydroxylase. It is the major neurotransmitter for the sympathetic nervous system, as well as for several sets of long axon, multiple-branched neurons (nerve cells) of the central nervous system. After release from nerve terminals onto its receptors, much of it is recaptured or removed from extracellular spaces by an uptake mechanism, or transporter, located in the nerve terminal membrane. This transporter is an important drug target for antidepressants and psychostimulants. Monoamine oxidase is a well-known enzyme that breaks down norepinephrine.

Norepinephrine holds an important place in the history of drug studies. It was discovered as an active chemical in the body many years ago. The availability of pharmacological agonists and antagonists helped reveal its physiologic role in the body. Also the development of histochemical methods in the 1960s and 1970s for its direct light microscopic visualization led to a detailed understanding of the many neurons that contain it. Noradrenergic receptors, termed alpha and beta, can act independently or synergistically to mediate the activity of norepinephrine and related drugs. Brain noradrenergic neurons in the nucleus locus ceruleus are well characterized in general and are activated during withdrawal from addictive drugs.

See also **Dopamine; Neurotransmitters; Receptor, Drug.**

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NORWAY. *See* **Nordic Countries (Denmark, Finland, Iceland, Norway, and Sweden).**

NUCLEUS ACCUMBENS. The nucleus accumbens is a group of neurons that is part of the limbic system and located near the midline in the frontal region, beneath the frontal lobe. Anatomically, it has been divided into the shell and core, with the shell perhaps being more important for the actions of drugs of abuse. It is one of the most important structures in the brain for studies of drug addiction because it is believed to be involved in reward, reinforcement, and unpredictably positive experiences. Nucleus accumbens is known to include neurons that contain GABA and acetylcholine and other neurotransmitters. It receives important input from dopaminergic neurons located in the ventral midbrain that are also involved in reward and reinforcement. It has output projections back to the ventral midbrain and other areas.

This nucleus is thought to be involved in the action of many different drugs of abuse, especially psychostimulants whose actions on the nucleus accumbens have been well studied. Destruction of

neurons in this structure or its inputs disrupts psychostimulant self-administration by rodents, and psychostimulants and other drugs of abuse cause an efflux of dopamine from this structure. Because of its small size, it has been difficult to study, and, at this time, it is being studied in humans and nonhuman primates to determine its relevance to human drug and stimulant abuse.

See also **Limbic System; Reward Pathways and Drugs.**

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NUTMEG. Nutmeg, the common spice obtained from the aromatic seed of the tree *Myristica fragrans* (native to the Moluccas, the spice islands of the East Indies), has been used for centuries for food and medicinal purposes. It causes some hallucinogenic activity when consumed in large amounts. Since nutmeg is found in most kitchens, including food preparation areas found in prisons, it has been used by prisoners. Therefore, it has been removed from ready access in prisons to the tighter control of drugs of abuse; Malcolm X wrote about such use.

Nutmeg contains elemicin and myristicin, whose structures have some similarities to the hallucinogen mescaline as well as to the psychostimulant amphetamine. It has been hypothesized that elemicin and myristicin might be metabolized in the body to form an amphetamine- and/or mescaline-like compound, but this has not been proven. The effects of nutmeg have been reported to have some similarities to those produced by marijuana; however, the large amounts of nutmeg that must be ingested to elicit behavioral effects can cause dry mouth and thirst, increases in heart rate, vomiting and abdominal pain, severe headaches, agitation, and panic attacks.

Figure 1. Nutmeg. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Lysergic Acid Diethylamide (LSD) and Psychedelics; Mescaline; Plants, Drugs From.**

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OBESITY. The term *obesity* derives from the Latin *obesus*, meaning "to eat up," and it came into use in English in the early 1600s to mean a condition characterized by excessive bodily fat. Excess body weight is associated with the increased storage of energy in the form of adipose tissue. Standard criteria for obesity are (1) greater than 20 percent above ideal body weight (IDW) for a given height, as determined from actuarial tables; or (2) body mass index (BMI), defined as weight in kilograms divided by height in meters squared (kg/m^2 = BMI), greater than 27 for men and greater than 25 for women.

The prevalence of obesity (in this case defined as having body fat in excess of 25 percent for males or 30 percent in females) is increasing worldwide, which varies substantially across ethnic groups and cultures and across age groups. In the United States, obesity is consistently more common among African American women than among white women; and tends to be more common among Hispanic women than among non-Hispanic women. Among men, race and ethnicity do not appear to play a significant role in the prevalence of obesity. Overall, approximately 90 million Americans are obese. In the early twenty-first century, the prevalence of obesity is leveling off in women but is increasing in men, children, and adolescents.

Obesity represents the upper end of a body-weight continuum rather than a qualitatively different state. Obesity can derive from a variety of causes (i.e., genetics, culture, nutritional intake, physical activity). Most notably, obesity is more prevalent (ten times more likely) in persons whose parents, brothers, or sisters are obese. Studies in identical twins have clearly demonstrated that genetics plays a major role. For example, nonidentical twins raised together were less similar in weight than identical twins raised apart. Environmental effects contribute to the rapid escalation and magnitude of the obesity epidemic in recent decades. The nature and nurture interactions for obesity are thought to occur after conception but before birth. Maternal nutritional imbalance and metabolic disturbances during pregnancy could affect gene expression and contribute to the development of obesity and diabetes mellitus of offspring in later life. Recent experiments have shown that nutritional exposures, stress or disease state after birth may also produce lifelong remodeling of gene expression.

Food ingestion is modulated by both peripheral and central signals. Peripheral hormone signals (e.g., ghrelin, cholecystokinin) that originate from the gut continually inform the brain about the status of acute hunger and satiety. The hypothalamus is a control center for appetite regulatory signals. The hunger peptide, ghrelin, normally increases during fasting. Ghrelin increases food intake and body weight by stimulating neurons in the hypothalamus. Its level is suppressed after a meal. Fasting ghrelin levels are lower in obese individuals and fail to decline after a meal, which may contribute to overeating. Obese individuals often have enlarged adipocytes with a reduced buffering capacity for fat storage. The dysfunction of adipose tissue plays an important role in the development

and progression of insulin resistance. Adipocytes modulate influx of dietary fat and secrete a variety of hormones (e.g., leptin). Leptin communicates the level of body fat stores to the brain and induces weight loss by suppression of food intake and by stimulation of the metabolic rate. Leptin is involved in the neuroendocrine response to starvation, energy expenditure, and reproduction (i.e., the initiation of human puberty).

Common forms of obesity in humans are failure of elevated leptin levels in the brain to suppress feeding and mediate weight loss, which is defined as leptin resistance. Leptin resistance in the hypothalamus invokes the starvation pathway and promotes food intake. The hedonic pathway that includes the ventral tegmental area and nucleus accumbens makes food intake rewarding. The nucleus accumbens is also referred to as the pleasure center of the brain, which is responsive to alcohol, morphine, nicotine, and cocaine. Leptin resistance in the brain reward pathway makes food intake a more potent reward and promotes the intake of palatable food.

Some researchers and clinicians see similarities among certain patterns of overeating and other excessive behaviors such as drinking too much alcohol, compulsive gambling, engaging in too much sexual activity, and even exercising compulsively. Some ingredients in palatable food (e.g., sugar) can be substances of abuse and lead to a natural form of addiction. For example, ingestion of sugar induces the brain to release opioids and dopamine. Dopamine is a neurotransmitter known to play a role in motivation as well as in the experience of reward and pleasure. In rats, certain circumstances (e.g., intermittent excessive sugar intake) can produce behavioral and neurochemical changes that resemble the effects of drug dependence. Eating and craving palatable food are reflexive reactions to stimulation of the reward pathway as evidenced in human brain imaging studies. Exposure to palatable food that cannot be consumed in fasting humans is associated with increases in striatal extracellular dopamine. Brain imaging of obese individuals shows a reduction in striatal dopamine D2 receptors, which is similar to the reduction reported in drug-dependent subjects. These findings could explain why aberrant eating behaviors observed in obese individuals resemble behavior related to drug dependence. Other mechanisms that govern eating behavior, such as stress, also underlie the development of obesity. Human studies show that acute stress increases snacking of high energy-dense food.

It should be noted that not all persons whose weight is above average are obese (they may have excess muscle mass); not all who are obese eat excessively; not all who eat excessively become obese; and some individuals who have clinically recognized disorders centered on eating and body weight, such as bulimia, may or may not be obese.

The prevention and treatment of obesity should be comprehensive, including pharmacological and lifestyle modification (e.g., education concerning nutrition and exercise, intensive family-based psychological counseling, and effective stress reduction) and surgical treatment (if indicated), in order to prevent health problems linked to obesity, such as hypertension, stroke, and type 2 diabetes mellitus.

See also **Bulimia Nervosa; Overeating and Other Excessive Behaviors.**

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OPERATION INTERCEPT. Described by government sources as the largest peacetime search-and-seizure operation in U.S. history, Operation Intercept was launched along the United States-Mexico border in September 1969. This unilateral program was instituted ostensibly to halt the flow of marijuana, heroin, and other dangerous drugs from Mexico into the United States. However, the actual goal of Intercept was not to interdict narcotics but to publicize the war on crime promoted by President Richard M. Nixon (served 1969–1974), who had taken office the previous January, and to force Mexican compliance with Washington's anti-drug campaign.

On September 16, 1968, presidential candidate Nixon had pledged to an Anaheim, California, audience that, if elected, he would move against the source of drugs and accelerate the development of tools and weapons to deter narcotics in transit. At the time, drug use per se did not elicit extreme concern from large segments of the population. According to a White House survey taken in May of 1969, people were more worried about racial problems, economic considerations, student unrest, and crime. In fact, among a substantial number of liberal-minded opinion leaders, some consensus was emerging that the prevailing 1950s-era drug legislation was too harsh, particularly with respect to marijuana. Nevertheless, among the Nixon constituency, the belief was common that drug use was increasing and that, with it, crime and antisocial behavior among youth was on the rise. Nixon's strategists must have seen narcotics control as an available strategy to move against crime and social unrest (both among minority populations and young people) and to divert attention from such problems as the war in Vietnam and the economy.

THE SPECIAL PRESIDENTIAL TASK FORCE

With John Ingersoll, the director of the Bureau of Narcotics and Dangerous Drugs, contending that the United States had "failed miserably" (*New York Times*, 1969, p. 23) in controlling narcotics abuse, Nixon chose to couple a highly publicized law-and-order campaign at home with an international offensive against foreign sources of heroin and marijuana. Attorney General John Mitchell was chosen to develop the program, and in April 1969 he and Treasury Secretary David M. Kennedy assembled a multiagency task force to form a plan to attack the importation into and illegal sale and use of illicit drugs in the United States. This Special Presidential Task Force Relating to Narcotics, Marijuana, and Dangerous Drugs consisted of two cochairmen, an executive secretary, and twenty members drawn from various departments in the government: Justice; Treasury; Defense; Agriculture; Commerce; Labor; Health, Education and Welfare: Transportation; the Coast Guard; the Interstate Commerce Commission; and the White House staff. Conspicuously absent was any representative from the State Department.

The Task Force Report, submitted to the president in June, established a linear relationship between marijuana, deteriorating health, heroin usage, and increased crime. It devoted its first fifteen pages to this argument. The remaining twenty pages examined what could be done to stop the flow of (mainly) marijuana across the border from Mexico. The last page of the report urged the State Department (absent from the deliberations as noted) to engage in a "massive, continuous effort, directed by the highest officials of Mexico, [to] significantly

curtail the production and refinement of marijuana and other dangerous drugs" (Special Presidential Task Force Report, 1969, p. 35). Officials noted further that (1) a significant percentage of the heroin was of Mexican origin; (2) substantial quantities of European heroin were being smuggled across the southern frontier; (3) Mexico served as an in-transit point for South American cocaine; and (4) considerable amounts of amphetamines and barbiturates entered the United States surreptitiously from Mexico. In the midst of so much smuggling, Mexico's resources and efforts remained inadequate. In the view of the task force report, both Mexican drug control statutes and the number of federal judicial police assigned to enforce them were insufficient. Mexican law enforcement authorities also lacked infrastructure and such technological resources as appropriate aircraft.

METHOD OF BORDER SURVEILLANCE

Something had to be done to elicit a concerted sustained anti-drug program from Mexico City. In July 1969 President Nixon sent a draft bill to Congress that would eventually become the Comprehensive Drug Abuse and Control Act of 1970. In August, the United States was flooded with media reports of a huge gathering of pot-smoking young music enthusiasts that would be remembered as Woodstock. In early September, the *New York Times* carried leaked reports of preparations for a spectacular operation to chokeoff cross-border smuggling from Mexico. On Sunday afternoon, September 21, 1969, at exactly 2:30 p.m. Pacific standard time, Operation Intercept was launched. Under the operational control of Myles Ambrose, the rather colorful commissioner of Customs, the operation was billed as "the largest search and seizure operation ever undertaken by civil authorities in peacetime" (*New York Times*, 1969, p. 29). Noting that the Mexican government had been kept "fully informed" of the operation, a U.S. Treasury Department news release termed Intercept a "coordinated effort" encompassing the law-enforcement resources of several branches of the federal government. Involving intensified land, sea, and air surveillance along the entire 1,945-mile U.S.–Mexico border, the effort would continue for an indefinite period, as everything and everyone, no matter their nationality or status, was thoroughly and painstakingly searched.

More than 4.5 million individuals and their belongings were ultimately inspected. Vehicles, their component parts, along with passengers' personal baggage, purses, books, lunch boxes, jackets, toys, and, in some cases, even blouses and hairdos were searched. The daily routine of life in Mexican border cities was radically altered, as traffic backed up for miles, car radiators boiled over, and tempers, both private and diplomatic, flared. No person or object, including diplomatic and consular officials, their children, possessions, and even their diplomatic cargo, was spared. In the process, the maneuver encompassed some two thousand personnel, intensified inspections, heightened air and sea surveillance, and the expenditure of some 30 million dollars.

On October 10, 1969, after some hasty negotiations with outraged Mexican officials (who did not feel that they had been fully informed), the administration announced that the border effort would be renamed Operation Cooperation. Surveillance was scaled back in return for a promise by Mexico to increase anti-marijuana enforcement and crop control.

Analyzed solely on the basis of drugs confiscated, Intercept surely was not worth the cost and effort it entailed. Seizures, however, were of minor importance.

In hindsight, the purpose of Operation Intercept appeared not to be to interdict drugs at the border but to press Mexico through economic denial. Seeking a politically expedient solution to the highly complex problem of domestic drug abuse and associated crime, the Nixon administration chose a course of action that, in effect, punished Mexico. Unfortunately, Intercept officials failed to gauge the impact of the blockage on the U.S. border economy. Highly dependent on shoppers and tourists from both sides of the border, U.S. and Mexican merchants reacted angrily and effectively through professional and civic groups. Pressure on the administration from border-state members of Congress was intense, and its impact increased as the project was prolonged. Along with diplomatic protests, this regional criticism proved crucial to Intercept's demise. The White House failed to recall the salient fact that Mexico is a foreign country and a friendly one at that.

Neglect of the State Department proved a serious blunder. Overlooked or overpowered by law-enforcement officials during Intercept's crucial

formative stage, U.S. diplomats ultimately terminated the ill-advised project before it became an even greater diplomatic disaster. More important, if its supporters had managed to prolong the unilateral maneuver for an extended period, U.S. authorities probably would have never secured the level of cooperation they sorely needed to impair the cultivation of drugs in Mexico and the trafficking of drugs across the border.

Additionally, the operation was poorly timed; it came on the eve of *tapadismo*, the process through which Mexico chooses its next president, but before the Nixon administration's announcement of a Latin American policy. Furthermore, Mexico played host during the Intercept period to a regional meeting of the United Nations Commission on Narcotic Drugs and the thirty-eighth annual assembly of Interpol, thereby compounding its embarrassment over the blockade's indignities.

Yet despite its numerous shortcomings, Operation Intercept was not entirely void of accomplishments. Because of the tremendous publicity it engendered, the program made Mexican officials keenly aware of a reality heretofore ignored or slighted: its own burgeoning drug problem. Politicians and journalists became introspective and reluctantly admitted that the availability of domestically produced drugs posed a danger to the health of *nuestra juventud* (our youth) as well as providing an everyday pastime for *gringo jippies* (American hippies).

Intercept also helped spur a previously lagging Mexican campaign against the cultivation, manufacture, and shipment of illicit drugs of all kinds. As a corollary to this effort, cooperation between Mexican and U.S. narcotics officials improved during the 1970s, but the 1985 kidnapping and murder of DEA agent Enrique Camarena in Guadalajara, Mexico, was tragic evidence of the daring and impunity with which traffickers continued to operate in the border area.

See also **Border Management; Crime and Drugs; Crop Control Policies; Drug Interdiction; International Drug Supply Systems; Mexico; U.S. Government Agencies: U.S. Customs and Border Protection (CBP).**

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OPIATES/OPIOIDS. The *opiates* are central nervous system depressants that are found in opium or are derived from a substance found in opium, which is the juice of the opium poppy (*Papaver Somniferum*). The *opioids* include the opiates, along with totally synthetic agents, and naturally occurring peptides that bind to one or more opioid receptors found in a number of animal species. In general usage, both terms are often used interchangeably—but opioids is the larger grouping.

The effects of opium have been known for several thousand years. For most of this time it was not clear which of the ingredients in opium provide its analgesic (painkilling) and other therapeutic properties.

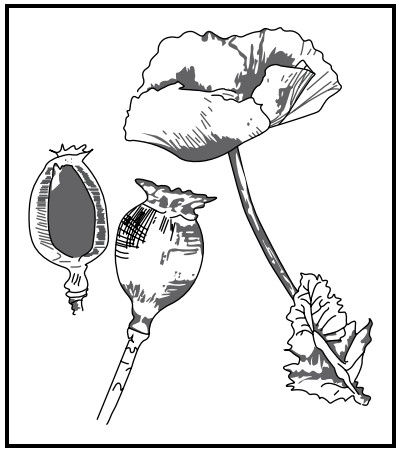


Figure 1. Opium poppy and pod. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Regardless of their benefits, health care providers are often afraid to prescribe opiods for fear of psychological dependence and sale to illegal markets (Carver, 2000). Still, the medical community has been increasing the use of opioid analgesics (Increasing Use, 2000).

Morphine and codeine, two of the most abundant constituents of opium, were the first pure opiates isolated—morphine in 1806 and codeine in 1832. Chemical modifications were soon attempted in an effort to eliminate their problematic side effects. One of the first attempts (in the 1890s) produced 3,6-diacetylmorphine, which is commonly known as heroin. This agent did not eliminate the problems of tolerance, dependence, or abuse. Since then, extensive studies of the important components of morphine's structure have led to the development of a number of different classes of organic compounds. In 1939 and 1940, the first synthetics were discovered. The recent discovery of the opioid peptides have provided even more diversity in drug design.

AGONISTS, ANTAGONISTS, AND PARTIAL AGONISTS

Some drugs have very complex actions and many drugs act at specific receptor, locations on the surface of a cell. All the drugs that belong to the class of drugs called opioids act at opioid receptors on the surface of cells. Usually these cells are neurons, but there are also opioid receptors on white blood cells. Once a drug binds to a receptor, it can either turn it on (agonist) or do nothing (antagonist). Even if a compound does nothing once it binds to the receptor, it still blocks the site and prevents an active compound from binding to the receptor. The situation is much like a key in a lock; some keys fit into the lock but will not turn, and as long as they remain in the lock they prevent the insertion of keys that would turn the lock. Finally, there are drugs known as *partial agonists*; these compounds bind to the receptor and turn it on but not nearly as well as pure agonists.

Again, using the key analogy, these partial agonists will turn in the lock, but only with some jiggling, lowering efficiency in opening the door. Pharmacologically, partial agonists have limited effects at the receptor, termed a *ceiling* effect. This means that increasing the dose further will not give a greater response. To further complicate understanding of these drug actions, it is important to recognize that the opioid receptors (and many other types of receptors as well) are actually families of similar but subtly different receptor types. Some opioids are agonists at one receptor type and partial agonists or even antagonists at another receptor type. These drugs are termed mixed agonist/antagonists and they can have complex pharmacological profiles. For this reason it can be difficult for pharmacists to determine conversion amounts (for example, to methadone) (Magill-Lewis, 2000).

RECEPTORS

Morphine and drugs with similar actions work through specific recognition sites, termed *receptors*, located on the outside of cells (see Table 1). A number of general classes of opioid receptors have now been identified and it is likely that even more will be discovered. The major types of opioid receptors have been designated mu, kappa, and delta. From the clinical perspective, the mu opioid receptors are the most important. This class, comprised of two subtypes, mu_1 and mu_2, have high affinity for morphine and most of the clinically used agents. Both mu subtypes mediate analgesia but through different mechanisms and locations within the brain and spinal cord. Mu receptors have been implicated in euphoria and mu agonists have often been abused. Equally important, activation of mu receptors depresses respiration and inhibits gastrointestinal transit. In addition to analgesia, euphoria, respiratory depression, and decreased activity in the stomach, mu agonist opioids produce some actions that are clinically useful, such as cough

Receptor	Agonists	Analgesia	Other action
Mu	Morphine		
mu_1		Supraspinal*	Prolactin release
			Acetylcholine turnover
mu_2		Spinal	Respiratory depression
			Inhibition of gastrointestinal transit
			Guinea pig ileum bioassay
Kappa			
$kappa_1$	Dynorphin A	Spinal	Diuresis
			Sedation (?)
			Rabbit vas deferens bioassay
$kappa_2$	Bremazocine		Pharmacology unknown
$kappa_3$	Nalorphine	Supraspinal	
Delta	Enkephalins	Spinal	Mouse vas deferens bioassay
			Dopamine turnover

*The supraspinal system is far more sensitive than the spinal one.

Table 1. Tentative receptor classification. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

suppression. However, most of their actions are considered unwanted side effects; for example, they affect endocrine function, constrict pupils, induce sweating, and cause nausea and vomiting. All mu agonist opioids also induce increasing tolerance and physical dependence in the user.

Kappa opioid receptors were defined using ketocyclazocine, an experimental benzomorphan derivative, and subsequently with dynorphin A, an endogenous opioid, which is believed to be the natural ligand for at least one of the kappa receptor subtypes. Morphine has relatively poor affinity for kappa receptors, but other drugs, such as pentazocine and nalbuphine (analgesics in clinical use), interact with kappa receptors quite effectively. The importance of kappa mechanisms in their actions has only recently been appreciated. The pharmacology of kappa receptors in humans has not been extensively studied; however, animal studies indicate that the kappa receptors also can relieve pain through receptor mechanisms distinct for each of the subtypes. Many of the clinically used drugs active at kappa receptors are mixed agonists/antagonists. Although they are agonists at kappa receptors, they are antagonists or partial agonists at mu receptors. In contrast to mu agonists, which can produce mood elevations and euphoria, drugs that activate kappa agonists appear to produce weird feelings and dysphoria.

The discovery of the enkephalins—endogenous peptides with opioid properties—soon led to the identification of delta receptors. The clinical pharmacology of delta receptors is not well known, primarily because so few agents have been tested in humans. Again, animal testing indicates an important role of delta receptors in analgesia, which is supported by a few studies with humans. However, there are no pure delta agonists clinically available as of 2008.

Although all the various receptor subtypes examined can relieve pain, each receptor represents a different mechanism of action. Their sites of action within the brain differ; and most importantly, agents highly selective for a specific subtype do not show cross-tolerance. While tolerance develops with continued activation of any of the various receptors, tolerance to one does not lead to tolerance to another. For example, tolerance to morphine does not diminish the response to a kappa or delta drug. Similarly, mu agonists produce a characteristic variety of physical dependence, and there is cross-dependence among mu agonists (that is, people dependent on heroin will not experience withdrawal if given methadone.) However, there is no cross-dependence between mu agonists and kappa agonists.

All the various subtypes produce a number of actions other than analgesia. Most of the nonanalgesic actions of opiates can be explained by considering the receptors to which they interact. An excellent example is mu_2 receptors, which mediate respiratory depression and the constipation seen with morphine. Drugs that are agonists at these receptors also produce these side effects while compounds lacking affinity for these receptors do not. The role of multiple receptors is important clinically, primarily since few drugs are specific for one receptor. Even morphine, which is highly selective for mu receptors, interacts with two mu subtypes, and at higher doses with delta receptors as well.

CLASSES OF OPIOIDS

Opioids can be divided into a series of classes based upon their chemical structures, illustrated by prototypic compounds from each group (see Figure 1). These include morphine and its close analogs, the morphinans, the benzomorphans, the phenylpiperidines, and methadone. The pharmacology of agents within each category can be quite varied and often can be predicted from their affinity for various opioid-receptor subtypes. Most of the clinically relevant drugs will interact with more than one receptor. Thus their actions can be ascribed to the summation of a number of receptor actions.

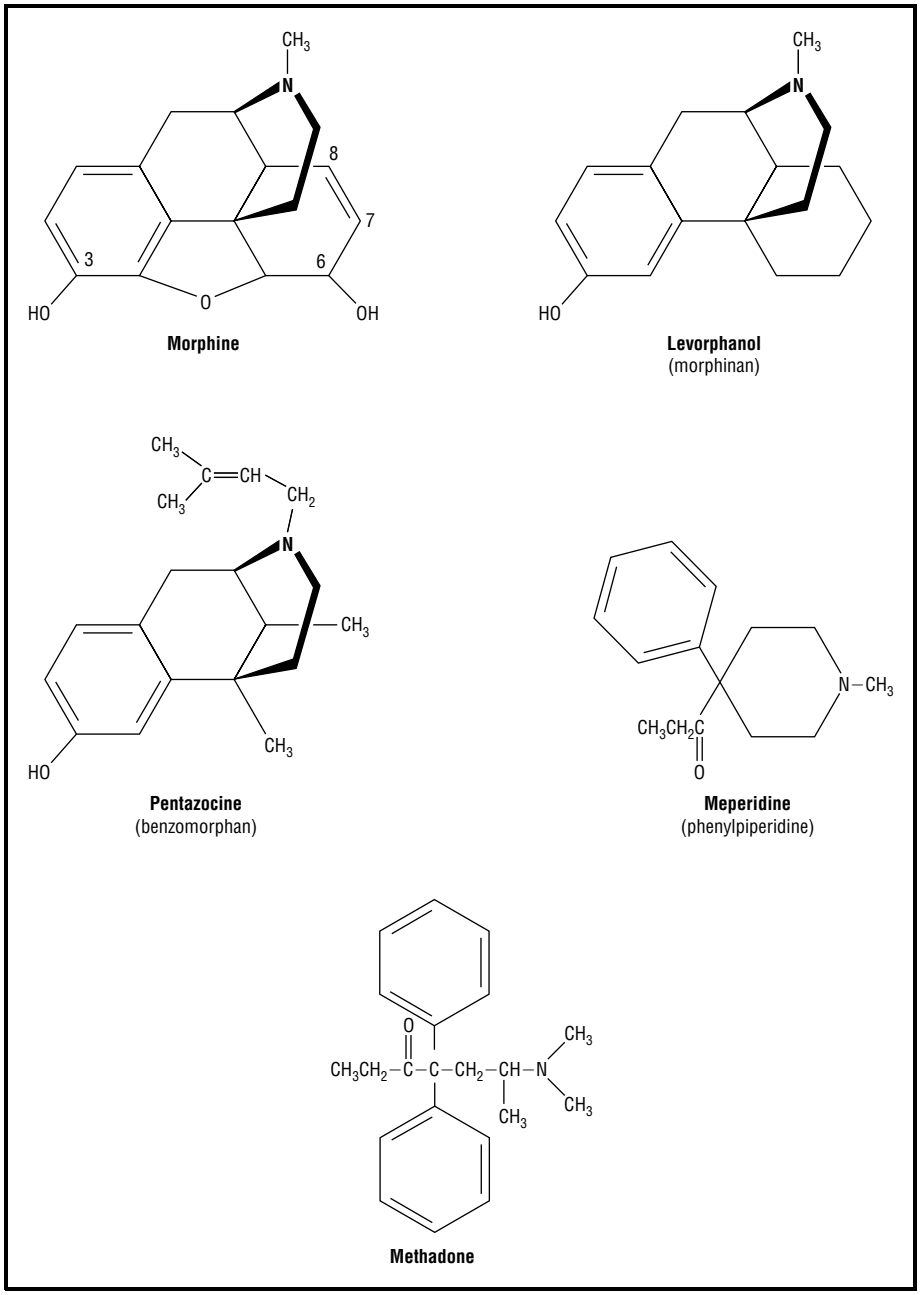
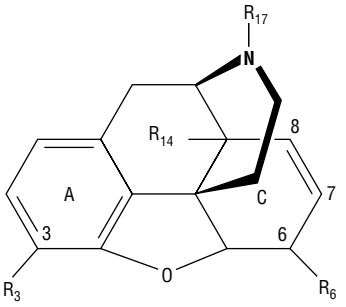


Figure 2. The classes of opioid compounds, based on structure. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The importance of various regions of the morphine molecule has been well studied and a number of related compounds are widely used (see Figure 2). Early studies examined small changes in morphine's structure. One of the critical groups is the hydroxyl group at the 3-position on the molecule. Blockade of this position by adding chemical groups markedly reduces the ability of the drug to bind to opioid receptors. Although this may seem at odds with the analgesic activity of codeine, which lacks a free hydroxyl group at the 3-position, evidence indicates that codeine itself is not active and is metabolized to morphine, which is responsible for its actions. A similar situation exists for oxymorphone and oxycodone.

The morphine molecule has a single nitrogen atom. The substituent on the nitrogen in these



Drug	R_3	R_6	R_{14}	R_{17}	C_6—C_7	Action
Morphine	OH	OH	H	CH_3	=	Agonist
Codeine	CH_3O	OH	H	CH_3	=	Agonist
Heroin	CH_3CO	CH_3CO	H	CH_3	=	Agonist
Oxymorphone	OH	=O	OH	CH_3	—	Agonist
Oxycodone	CH_3O	=O	OH	CH_3	—	Agonist
Hydromorphone	OH	=O	H	CH_3	—	Agonist
Naloxone	OH	=O	OH	$CH_2CH=CH_2$	—	Antagonist
Nalbuphine	OH	OH	OH	CH_2—◇	—	Ag/Antag
Nalorphine	OH	OH	H	$CH_2CH=CH_2$	—	Ag/Antag

Figure 3. The morphine molecule and some widely used related compounds, based on the region of the molecule. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

series of opiates can have major effects on activity. Morphine and most of the mu agonists contain a methyl (CH_3-) group on the nitrogen, but a number of other compounds with different substituents have been developed. Replacing the methyl group with an allyl ($-CH_2CH=CH_22$) or methylcyclopropyl ($-CH_2CHCH_2CH_2$) group does not have much effect upon the ability of the compound to bind to opioid receptors, but it markedly changes what happens when they do bind. For example, oxymorphone, with its methyl group on the nitrogen, is a clinically useful analgesic many times more potent than morphine. Replacing the methyl group with an allyl group produces naloxone. Naloxone is an antagonist, a drug that blocks or reverses the actions of other opiates. Clinically, naloxone is used as an antidote to opiate overdose. This drug's structure shows how simple changes can profoundly influence the pharmacology of these agents.

Further investigations revealed that Ring C of morphine can be eliminated, enabling use of the benzomorphans—many of which are potent analgesics. The major drug in this group is pentazocine (Talwin). Even simpler structures produce potent analgesics, such as methadone. The phenylpiperidines comprise another large group of opioids. The first of these to be used clinically was meperidine, which was first prescribed in 1939 and which still is extensively used. Modifications of the phenylpiperidine structure led to a subgroup of drugs, with fentanyl as a prototype. Fentanyl is approximately 80-fold more potent than morphine, but its very short duration of action requires continual infusions. An advantage is that once the infusion is discontinued, the effects of the drug clear rapidly. This ability to quickly turn on or off the drug's actions, along with its great potency, has made this agent a valuable tool in anesthesia. This high potency has been exploited to develop skin patches that give a constant release of fentanyl into the body as the drug is absorbed through the skin. Other agents within this series, such as sufentanil and alfentanil, are even more potent than fentanyl. Two other members of this series, loperamide and diphenoxylate, have activity but very poor solubility. This property has led to their use as antidiarrheal agents since they cannot be made soluble and injected and are therefore less likely to be abused.

Together, these structure activity studies reveal that the basic requirements needed for opioid activity are quite simple. However, the wide variety

[Leu^5]enkephalin	**Tyr-Gly-Gly-Phe-Leu**
[Met^5]enkephalin	**Tyr-Gly-Gly-Phe-Met**
Dynorphin A	**Tyr-Gly-Gly-Phe-Leu**-Arg-Arg-Ile-Arg-Pro-Lys-Leu-Lys-Trp-Asp-Asn-Gln
Dynorphin B	**Tyr-Gly-Gly-Phe-Leu**-Arg-Arg-Gln-Phe-Lys-Val-Val-Thr
α-Neoendorphin	**Tyr-Gly-Gly-Phe-Leu**-Arg-Lys-Tyr-Pro-Lys
β-Neoendorphin	**Tyr-Gly-Gly-Phe-Leu**-Arg-Lys-Tyr-Pro
β_h-Endorphin	**Tyr-Gly-Gly-Phe-Met**-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-Phe-Lys-Asn-Ala-Ile-Ile-Lys-Asn-Ala-Tyr-Lys-Lys-Gly-Glu
Dermorphin	Tyr-D-Ala-Phe-Gly-Tyr-Pro-Ser-NH_2

Table 2. Selected opioid peptides. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

of structures becomes even more intriguing since morphine and the other opioids act within the brain by mimicking naturally occurring peptides—the endogenous opioids. The enkephalins were the first such naturally occurring substances to be isolated and sequenced (Table 2). Initially, these results were somewhat confusing since the two enkephalins—both pentapeptides—contain the identical first four amino acids and differ only at the fifth. The complexity of these peptides became more clear with the subsequent isolation and characterization of β-endorphin, a 31-amino acid peptide derived from a larger protein, which also gives rise to active compounds, including ACTH and α-MSH. The first five amino acids in β-endorphin are identical to [met^5]enkephalin, but [met]enkephalin and β-endorphin derive from different gene products. There are also a series of compounds containing the sequence of [Leu^5]enkephalin, including dynorphin A, dynorphin B and α-neoendorphin. All these compounds (the enkephalins, endorphins, and dymorphine) have distinct genes and are expressed independently from one another. Thus, they comprise a family of similar but discrete neurotransmitters.

The opioid peptides are becoming important clinically. A major difficulty in the use of peptides is the fact that they are broken down when taken by mouth; thus most have very limited oral activity. However, new derivatives specifically designed to be more stable have been developed, which will provide new leads. The enkephalins are potent at delta receptors, and many of their derivatives are delta-selective. Some of the more recent derivatives label delta receptors more than 10,000-fold more selectively than others. Yet other peptides are very much like morphine in terms of their pharmacology and receptor binding. Finally, peptides with opioid actions are now being identified in a variety of other tissues; for example, toad skin has dermorphin, a potent and stable opioid peptide.

See also **Addiction: Concepts and Definitions; Opioid Complications and Withdrawal; Pain, Drugs Used for.**

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Will opium rear its smoky head yet again? (1999). *Psychopharmacology Update, 10*, 3.

GAVRIL W. PASTERNAK

OPIOID COMPLICATIONS AND WITHDRAWAL. Opioids are frequently used in medicine for pain relief. The most commonly used opioids include morphine sulfate (Duramorph, MS Contin, Roxanol), meperidine (Demerol), hydromorphone (Dilaudid), oxymorphone (Numorphan), methadone (Dolophine), codeine phosphate and codeine sulfate, oxycodone (Percocet, Percodan), and hydrocodone (Hycodan, Vicodin). However, these substances are also among the most common drugs of abuse. When taken under medical supervision, opioid drugs have a low level of serious toxicity, with the most common side effects being nausea, drowsiness, and constipation. When self-administered, however, and not taken under medical supervision, their use is associated with a high incidence of untoward actions and side effects, as well as with a high death rate when used alone or in combination with other drugs (including alcohol).

A 2005 report by the Drug Abuse Warning Network (DAWN) estimated that heroin was involved in 164,572 emergency room visits in the United States in 2005. The DAWN report also found that in 2003 the rate of opiate-related drug abuse deaths in six states was in the range of 7.2 to 11.6 per 100,000 people.

RESPIRATORY DEPRESSION

It is generally believed that the most common life-threatening complication of opioid use, whether therapeutic or illicit, is respiratory depression, or loss of the ability to breathe automatically. Probably the most important action of morphine-like drugs in producing respiratory depression is the lessening of the sensitivity and responsiveness of the brain's medullary respiratory center to carbon dioxide (CO_2—the metabolic waste that circulates in the blood, derived from carbonic acid during animal respiration). Therefore, CO_2 becomes an inefficient respiratory stimulant, and automatic breathing ceases.

Administering a specific opioid antagonist such as naloxone to patients with severely depressed respiration frequently produces a dramatic increase in the rate of respiration and the volume of air taken in per breath. This occurs when a partial or completely re-sensitized respiratory center is confronted with high brain levels of CO_2. When the brain CO_2 levels dissipate as a consequence of the evoked excessive rate and volume of breathing (hyperpnea), the volume of air breathed per minute decreases. Yet when brain levels of the antagonist decrease, the respiratory depressant action of the opioid may again assert itself. Naloxone is a relatively short-acting antagonist (blocker). Patients who, for example, have received an overdose of long-acting opioids (e.g., methadone) may experience a fatal respiratory depression following an initially successful treatment with naloxone because the administration of that drug was discontinued prematurely.

TOLERANCE AND PHYSICAL DEPENDENCE

Other complications associated with the chronic use of opioids are the development of tolerance and dependence.

Tolerance. The most common understanding of tolerance to opioid drugs is that following chronic administration of one of these drugs, its effects are diminished. Several mechanisms are involved in the development of tolerance to drugs, including: (1) the induction of drug-metabolizing enzymes, (2) the development of coping strategies, (3) the exhaustion or depletion of neurotransmitters, and (4) an alteration in the number of active and inactive receptors. However, these mechanisms have, by and large, failed to provide adequate explanations for tolerance to opioid drugs. This may stem in part from the complexity of the results of chronic administration of opioids, the involvement of multiple mechanisms, and the influence of the dose, route, and frequency of drug administration.

Opioids, for example, alter the functioning of some body mechanisms that maintain homeostasis (i.e., equilibrium), and apparent tolerance is related to the establishment of new equilibrium conditions. This is clearly evident in respiratory depression, where opioids depress both the sensitivity and the reactivity of the brain-stem respiratory CO_2 homeostat (the sensor involved in maintaining homeostasis), causing CO_2 to be a less effective respiratory stimulant. Yet when CO_2 accumulates because of depressed respiration, the increasingly higher concentrations will cause stimulation of respiration to the degree that the altered homeostat dictates. The ability of opioids to constrict pupils (i.e., make them smaller) is dose-related, and patients receiving opioids frequently have miosis

(near maximally constricted pupils). It is therefore difficult to determine if tolerance develops to opioids' miotic effect. This has given rise to the commonly accepted view that tolerance does not develop to the miotic effects of opioids.

In former opioid addicts, morphine-like drugs produce dose-related feelings of enhanced self-image, of being more efficient and effective, and of well-being. These related subjective states form the essence of opioid-induced euphoria, which is produced in patients who are plagued by feelings of inadequacy. This can be quantitatively measured using the Morphine-Benzedrine Group scale of the Addiction Research Center Inventory (ARCI).

Tests in many normal subjects (nonabusers) who are not suffering from pain indicate that opioids do not produce euphoria. Instead, in sufficiently large doses, they produce feelings of apathy and ineffectiveness, which can be dispiriting (dysphoric). When opioids are administered chronically to addicts, the subjective effects they produce change from feelings of well-being to feelings of being withdrawn, tired, and weak. With regard to these effects of chronic opioid administration, the effects are not simply diminished but rather changed.

The development of tolerance can be a problem when opioids are used in the treatment of pain. Although some degree of tolerance to analgesic effects is expected when opioid drugs are used repeatedly, in practice there is a great deal of variability among patients. Some patients with cancer pain appear to derive satisfactory relief from the same dose of morphine or similar drugs over a period of many months. For these patients, a need to increase the dose can be a signal that the disease is progressing. Other patients with terminal disease can develop remarkable tolerance. There are reports of patients who have been given the equivalent of 1,000 milligrams of morphine per hour intravenously. This is an impressively large dose, since the usual starting therapeutic doses of morphine are 10 to 15 milligrams by injection every 4 to 6 hours, and doses of more than 60 milligrams by injection can cause potentially fatal respiratory depression in nontolerant individuals. It is not usually of much benefit to change to another opioid that acts at the same receptor. For example, morphine acts at the mu-opioid (or μ-opioid) receptor. When tolerance develops to morphine, other opioids acting at mu receptors will be less effective, a phenomenon referred to as "cross-tolerance."

Physical Dependence and Withdrawal. Closely related to the phenomenon of tolerance is the phenomenon of physical dependence. Subjects given repeated doses of opioid agonists (which act on opioid receptors to trigger physiologic actions similar to the body's natural chemicals that act at those receptors) exhibit a syndrome when the drug is withheld or when the subject is administered an opioid antagonist. The resulting group of signs and symptoms is called the "withdrawal syndrome" or "precipitated abstinence syndrome." Subjects who exhibit an abstinence syndrome are said to be "physically dependent" on the opioid. The degree of physical dependence and the intensity of the abstinence syndrome are related to the dose of the opioid agonist chronically ingested. In general, the intensity of all signs and symptoms vary together.

The opioid withdrawal syndrome includes restlessness, weakness, chills, body and joint pains, gastrointestinal cramps, anorexia (loss of appetite), nausea, feelings of inefficiency, and social withdrawal. Signs of withdrawal are generally opposite those of the acute effects of a drug, and for opioids they include activation of the autonomic nervous system, yawning, lacrimation (tearing eyes), rhinorrhea (running nose), piloerection (gooseflesh), tachypnea (rapid breathing), mydriasis (dilated pupils), hypertension (high blood pressure), tachycardia (rapid heart beat), muscle spasms, twitching, restlessness, vomiting, and diarrhea. The waves of gooseflesh that occur during severe opioid withdrawal remind some observers of the look of a plucked "cold turkey," a term that has come to be used not only for any abrupt discontinuation of a drug, but also for sudden cessation of any habit or pattern of behavior. The twitching and kicking movements of the lower extremities that can occur during opioid withdrawal have given the English language another widely used term, "kicking the habit," which is used to denote the process of giving up any pattern of behavior or drug use.

The time of onset of opioid withdrawal depends on the length of activity for the dependence-producing opioid. The withdrawal syndrome of subjects dependent on morphine or

heroin is well developed within 24 hours after the last dose of the opioid, peaks after 48 hours of abstinence, and gradually subsides thereafter. Signs of abstinence in patients dependent on methadone begin to emerge 24 to 48 hours after the last dose and may not peak for two weeks.

After this acute withdrawal syndrome subsides, a protracted abstinence syndrome emerges. This differs from the acute withdrawal syndrome in some ways but not in others. Subjects who are dependent on morphine or methadone show the following signs of protracted abstinence: a modest hypotension (low blood pressure), bradycardia (low heart rate), hypothermia (lower than normal body temperature), miosis (small, constricted pupils), and tachypnea. Other signs of protracted abstinence may include an inability to concentrate and a decrease in fine-motor control. Symptoms associated with protracted abstinence in patients who were dependent on methadone include feelings of tiredness and weakness, withdrawal from society, inefficiency, decreased popularity and competitiveness, and loss of self-control. Protracted abstinence persists for at least 25 weeks after withdrawal. Protracted abstinence following addiction to morphine has also been demonstrated in rats and in dogs.

The patterns of withdrawal and the time course of symptoms described above are seen when opioid drugs that have been used for weeks or months are discontinued. However, opioid withdrawal can also be observed when a drug-dependent person is given an opioid antagonist (a drug such as naloxone that competes with opioid agonists for the opioid receptor). In a matter of minutes, this will produce a precipitated abstinence syndrome that can be severe, with vomiting, cramps, and diarrhea. This precipitated abstinence is usually brief, however, because as soon as the antagonist is metabolized (usually less than an hour for naloxone), the opioids still in the body can again attach to the opioid receptors and suppress the abstinence syndrome.

The biological mechanisms that are responsible for the development of opioid physical dependence are set into motion with the very first doses of an opioid drug. If volunteer subjects are given standard doses of morphine (15 to 30 mg) and then, after an interval varying from 6 to 24 hours, they are given naloxone, they report nausea and other feelings of dysphoria and exhibit yawning, dilated pupils, tearing, sweating, and runny nose. Changes in endocrine levels are also seen that are similar, although not as extreme, as those seen when chronically administered opioids are abruptly discontinued.

SIDE EFFECTS OF OPIOIDS

As mentioned previously, there are a number of side effects commonly associated with the use of opioid analgesics, including nausea, constipation, itching, convulsions, and dysphoria.

Nausea and Vomiting. Nausea and vomiting are experienced following the administration of opioids orally, by injection, or by injection into the spinal canal (epidurally), and they are worsened by movement and the resulting stimulation of the vestibular system (inner ear organ responsible for balance). The site responsible for these actions of opioids is presumed to be a special area in the brain stem or medulla, the chemoreceptive trigger zone of the area postrema.

Constipation. Constipation, a common but undesirable effect of opioids, is sometimes a useful effect for which opioids can be prescribed. It is undesirable when opioids are used for the relief of pain and in opioid-dependence maintenance therapy. This effect of opioids can be used to advantage, however, to treat diarrhea. In fact, the oldest of the therapeutic actions of opiates is their antidiarrheal and constipating effects.

It is now known that the extrinsic innervation (nerves leading from the central nervous system to the gut) and the intrinsic innervation (nerves within the wall) of the gastrointestinal (GI) tract are complex and vary from species to species. A variety of neurons with diverse neurotransmitters have been identified in the GI tract, including neurons and their processes that contain opioid peptides: the enkephalins, beta-endorphin, dynorphins, and other ligands derived from pro-opiomelanocortin. Further, mu and delta opioid receptors have been identified in the GI tract. The vagus nerve also has fibers that contain enkephalins, and the central nervous system has opioid mechanisms that modulate GI movement (motility).

Several influences must play a role in the constipating effects of opiate agonists, including increased segmental activity, decreased propulsive

activity, and decreased secretory activity. Naloxone, even when administered in high doses for a long period of time in antagonist therapy of opioid abusers, does not produce an overt stimulation of the GI tract resulting in diarrhea. When opioid antagonists are administered to opioid-dependent subjects, however, GI cramps and diarrhea develop as classic opioid withdrawal signs.

Pruritus. The ability of morphine-like drugs to produce the sensation of itching (pruritus) is well known, and it is a discomforting complication when opioids are administered for therapeutic reasons. Further, many morphine-like drugs (e.g., codeine) release histamine from white blood cells that store it (mast cells and basophils). When morphine is administered intravenously, wheals (hives, or raised red lumps) may appear at the site of the injection and along the course of the vein. The wheals may be associated with the sensation of itching. Occasionally, large doses of morphine may produce generalized itching. Rarely, morphine produces pulmonary edema (fluid in the air sacs of the lung), bronchoconstriction (narrowing of the air tubes in the lungs), or wheezing. With the advent of the use of intrathecal and epidural morphine (injection of morphine into spinal fluid or around the lining of the spinal canal) in pain management, the incidence of morphine-induced pruritus has become greater. Under this circumstance, the distribution of itching may be segmental (limited to the part of the spinal cord involved). Itching remains an elusive phenomenon and is harder to define and investigate than pain. It is thought that it may be mediated by a subgroup of nociceptive (pain-carrying) C nerve fibers. Further, morphine's histamine-releasing property has been implicated in its ability to produce itching, as histamine does in allergic reactions.

Convulsions. Although most opiates produce convulsions when administered in very large doses, convulsions are most frequently observed when excessively large doses of meperidine (Demerol) or *d*-propoxyphene (Darvon) are administered. Emergent meperidine seizures are characterized by tremors and twitching, which may evolve into tonic-clonic (epileptic) convulsions. Focal and tonic-clonic seizures have been observed in patients overdosed with *d*-propoxyphene. The mechanisms whereby opioid drugs produce convulsive phenomena are not well understood and may involve several mechanisms, including: (1) direct and indirect dysinhibition of glycine and GABA-mediated inhibition, and (2) excitatory actions that are probably mediated by yet-to-be-classified receptors. The convulsant effects of *d*-propoxyphene can be readily antagonized by naloxone; however, meperidine's convulsant effects may be more resistant. Meperidine probably has a convulsant effect in its own right when administered in very large doses acutely, yet convulsant phenomena seen following the administration of multiple doses of meperidine are produced by the accumulation of a metabolite, normeperidine.

Dysphoria, Delusions, and Hallucinations. It is rare for morphine-like analgesics to produce psychotic reactions. In patients with severe pain and discomfort and in opiate addicts, single doses of morphine-like drugs most commonly produce feelings of well-being. In normal subjects with no pain or with only modest levels of discomfort, morphine produces feelings of apathy and enervation, which are somewhat dysphoric. The drug *d*-propoxyphene (Darvon) has been reported to produce bizarre reactions—delusions and hallucinations—particularly when taken chronically in large doses and when used to suppress opioid abstinence. Some agonists-antagonists (e.g., pentazocine [Talwin], nalorphine, and cyclazocine) produce feelings of apathetic sedation, perceptual distortions, anxiety, delusion, and hallucinations.

STREET DRUGS

The complications described in the preceding sections are most commonly associated with pure, unadulterated opioids. When street drugs, which are typically diluted by the seller with quinine, lactose, or other powdered materials, are injected by the user in an unhygienic manner—in doses that vary significantly—the range of complications widens. Among the complications of heroin use reported in the medical literature are strokes, inflammation of cerebral (brain) blood vessels, toxic amblyopia (painless loss of vision caused by a toxic insult to the optic nerve), bacterial meningitis (infection and/or inflammation of the tissue covering the brain), aneurysms (bulging blood vessel) and brain abscesses (area of localized infection in the brain), disorders of peripheral nerves, impairment of

segments of the spinal cord, and widespread injury to muscle tissue (rhabdomyolysis)—which by releasing muscle protein can cause damage to the kidneys.

OTHER MEDICAL COMPLICATIONS

Medical complications of opioid addiction may result from unsanitary administration of the drug, from overdosing, from intoxicated behavior (e.g., accidents, unsafe sex), or from the chemical properties of opioids themselves.

Lungs. Opioid addiction may lead to pneumonia, aspiration pneumonitis (inflammation of the lung tissue from inhaling vomit or other secretions), lung abscess (an area of localized infection within the lung), or septic emboli in the lungs (an infection that starts in the cardiovascular system but spreads via the blood stream and lodges in the lung tissue). It also decreases the vital capacity and diffusion capacity of lung tissue. Opioid addicts who also smoke tobacco are at increased risk of lung infections.

Liver. Opioid addicts frequently develop viral hepatitis (types A, B, and C). In addition, addicts who are also heavy drinkers have a high incidence of cirrhosis and other disorders of liver function.

Immune System. Hypergammaglobulinemia (an abnormally high level of gamma globulin in the blood) develops in about 90 percent of opioid addicts. It is unclear whether this change in the immune system is caused by infections or by daily injections of foreign substances. It diminishes in addicts on methadone maintenance. In addition to hypergammaglobulinemia, opioid addicts are at a very high risk of contracting HIV infection from shared needles.

Muscles and Bones. Osteomyelitis (inflammation of bone and the bone marrow caused by bacterial infection) is a common complication of opioid addiction. Drug abuser's elbow is a complication in which the muscles of the lower arm are damaged by repeated needle punctures and tears.

Skin and Lymphatic System. Opioid addicts frequently develop skin abscesses and ulcerated areas from injecting heroin under the skin ("skin popping"). Using contaminated needles may result in cellulitis (an infection of the skin), lymphangitis (inflammation and infection of the lymphatic system), lymphadenitis (infection of the lymph nodes), and phlebitis (inflammation of a major vein).

Pregnancy and Lactation. Because both heroin and methadone cross the placental barrier, infants of opioid-addicted mothers are born physically dependent on the drug. They may also acquire HIV infection or hepatitis from an infected mother. Pregnant addicts should be encouraged to enter a methadone maintenance program rather than attempt complete withdrawal, because withdrawal in the last trimester of pregnancy may cause early labor. Mothers on methadone can nurse infants without harm to the child, because breast milk will not contain large amounts of methadone. Buprenorphine is an opioid partial agonist that is approved for the treatment of opioid dependence. Because the use of buprenorphine in pregnancy is less well studied than that of methadone, the latter is presumed to be safer.

THE TREATMENT OF OPIOID WITHDRAWAL (DETOXIFICATION)

The opioid withdrawal syndrome varies in severity depending on the amount of opioid used and the duration of use. For the average user of illicit opioids, withdrawal is rarely severe because the amount of drug used typically is not high. The withdrawal syndrome from such a level of use can be uncomfortable, but it is not life threatening in otherwise healthy individuals. However, death can occur if severe withdrawal is left untreated in individuals who are weakened by other medical conditions.

The process of treating someone who is physically dependent so that acute withdrawal symptoms are controlled and the state of physical dependence is ended is usually referred to as detoxification. For opioid drugs, this process can be managed on an ambulatory (outpatient) basis or in a hospital or other residential (inpatient) setting. The most common approach to easing the severity of opioid withdrawal is to slowly lower the dose of opioid over a period of days or weeks. In the United States, however, if the drug is heroin, a substitution technique is used instead. Since virtually all opioids that are abused act as agonists at the mu-opioid receptor, any mu agonist could be a suitable substitute, but the only full agonists to be approved for

this purpose in the United States are methadone and LAAM (L-alpha-acetylmethadol). These medical agents are effective when taken by mouth. Methadone can completely suppress the opioid abstinence syndrome. This capacity of one opioid to prevent the manifestations of physical dependence from another is called cross-dependence. LAAM, however, was recently withdrawn from the market because of deaths linked to a toxic action of the drug on cardiac function, which was thought to cause sudden death in some patients. Buprenorphine, a partial mu agonist, has also been approved for the treatment of opioid withdrawal.

Outpatient detoxification using methadone typically involves using doses of 20 to 40 milligrams per day for a few days and then gradually reducing the dose over several weeks. Because so many patients return to illicit drug use as the dose of methadone approaches zero, government regulations controlling methadone permit a long period (up to 180 days) of slow dose reduction.

When detoxification takes place in a hospital or other residential setting, where the patient is presumably not as likely to be exposed to environmental cues that elicit craving for opioids, dose reductions of methadone can be more rapid (e.g., over 8 to 10 days), although the intensity of discomfort will be higher.

Buprenorphine (Suboxone, Subutex) a partial mu agonist, and L-alpha-acetylmethadol have also been used satisfactorily to facilitate detoxification. The opioid withdrawal syndrome can also be modified and reduced in severity by treatment with medications that do not act at the mu receptor, but instead act on some of the physiological systems that cause hyperactivity as part of the syndrome. The use of the antihypertensive medication clonidine (Catapres) is an example. Additional supportive pharmacotherapies have been aimed at reducing withdrawal symptoms through peripheral routes, such as dicyclomine (Bentyl) for abdominal cramping, loperamide (Immodium) for diarrhea, and methocarbomal (Robaxin) for muscle cramping. Psychopharmacologic agents, such as atypical antipsychotics, may be used in patients with a serious co-occurring psychiatric disorder in order to reduce anxiety, insomnia, mood instability, and psychosis during withdrawal.

The opioid antagonist naltrexone can be used to detoxify patients rapidly and to help detoxified addicts stay off opioids. Naltrexone binds more strongly than heroin to the specific brain receptors to which heroin binds. The withdrawal is usually more severe than that which comes from simply stopping the heroin, but it also has the effect of detoxifying the individual more quickly. Thus, a combination treatment of clonidine to suppress the intensity of withdrawal symptoms and naltrexone to accelerate the pace of withdrawal has been used for rapid detoxification. An ultrarapid detoxification procedure that uses opioid antagonists and other medications administered while the patient is under general anesthesia has been used to detoxify patients from opioids, but the safety, efficacy, and advantage of this method, compared to more conservative methods, has yet to be clearly demonstrated. Ultrarapid opioid detoxification remains controversial because it may be associated with increased morbidity and mortality.

Because opioid withdrawal is time-limited and rarely life threatening, many nonmedical treatments have also been used, including acupuncture and herbal medicines. Another nonmedical treatment that has been used in addicts is transcutaneous electrical nerve stimulation (TENS). It is thought that both acupuncture and TENS may be helpful because they stimulate the parts of the central nervous system that release natural opioids. At present, further research is needed because opioid addicts are very suggestible and may feel better after acupuncture or TENS because of the placebo effect.

See also **Addiction: Concepts and Definitions; Agonist; Agonist-Antagonist (Mixed); Antagonist; Brain Structures and Drugs; Complications; Drug Abuse Warning Network (DAWN); Drug Types; Heroin; L-Alpha-Acetylmethadol (LAAM); Memory, Effects of Drugs on; Methadone Maintenance Programs; Morphine; Naloxone; Naltrexone; Neurotransmitters; Opiates/Opioids; Opioid Dependence: Course of the Disorder Over Time; Opium: U.S. Overview; Pain, Drugs Used for; Physical Dependence; Pregnancy and Drug Dependence; Receptor, Drug; Tolerance and Physical Dependence; Treatment: An Overview of Drug Abuse/Dependence; Treatment, Pharmacological Approaches to: An Overview; Treatment, Pharmacological Approaches to: Buprenorphine; Treatment, Pharmacological Approaches to: Methadone; Treatment, Pharmacological Approaches to: Naltrexone; Treatment, Specialty Approaches to:**

Acupuncture; Wikler's Conditioning Theory of Drug Addiction; Withdrawal.

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OPIOID DEPENDENCE: COURSE OF THE DISORDER OVER TIME.

Opioid is the term used to describe a chemical agent whether naturally derived or synthetic that activates opioid receptors in the brain and in other locations throughout the body. Examples of opioids include the naturally occurring products codeine and morphine as well as the semi-synthetic street drug heroin and the totally synthetic drug methadone. For the topic of opioid abuse and dependence, the most relevant receptors are those located in the reward circuitry of the brain and those located in the gastrointestinal tract. When opioids are ingested, these opioid receptors are activated. The response in the brain is a feeling of calm euphoria and a sense of wellbeing. The reinforcing effects promote repeated use. Simultaneously,

the receptors in the GI tract are activated, which slows down propulsive movement and produces constipation. Although there are many other effects such as pain relief, constriction of the pupil of the eye, sedation and depressed breathing, the euphoric effects in the brain and the constipating effect in the gut are the most relevant to the development of addiction and the experience of withdrawal distress.

OPIOID DEPENDENCE DEFINED

Substance Related Disorders are classified in the *Diagnostic and Statistical Manual of Mental Disorders* (4th edition) referred to as DSM-IV. Opioid dependence describes the condition commonly known as *narcotic addiction*. This diagnosis is reserved for the condition in which a compulsive, repetitive, destructive cycle of drug use continues despite adverse consequences. The inconceivable situation in which a person who has achieved a period of abstinence, often after experiencing severe, painful withdrawal distress and making sincere pronouncements of intentions to quit for good, relapses to yet another bout of opioid abuse is perhaps the most frustrating aspect of attempts to understand this condition.

Opioid dependence is regarded by the American Medical Association (AMA) as a primary, chronic, progressive, relapsing, fatal disease. This conceptualization is in sharp contrast to the widespread view in the general population and the desperate desire among opioid addicts to believe that getting over an addiction is simply a matter of achieving abstinence from the drug. The course of opioid dependence over time is marked by an insidious decline into a destructive, compelling relationship with opioids. The recovery from this condition requires no less than a total commitment to a life that rejects all the activities and trappings associated with substance abuse.

EXPERIMENTATION AND TOLERANCE

No one experiments with opioids intending to develop an addiction, yet about 25 percent of those who try opioids even one time will do so. The path from experimentation to addiction begins with curiosity about the effects of the drug or possibly ingestion motivated by peer pressure. If the reward from this initial exposure exceeds the negative consequences, the individual may engage in subsequent use with continued reinforcing effects. Over a period of weeks, months, or perhaps years, individuals continue a pattern of increasingly frequent use, being drawn back to the drug experience for its positive effects or because the drug relieves angst or emotional distress. Individuals may eventually become convinced that opioid use makes life more pleasant and its continued use becomes integrated into their pattern of life. Infrequent, occasional use yields to a regular pattern of self-administration, which leads to drug tolerance.

Tolerance, a physiological adaptation, in turn requires larger doses to achieve the desired effect. Although tolerance is always present in individuals with physical dependence, the two can be readily differentiated. The user who has progressed into the condition of physical dependence finds that reduced use is met with abdominal distress and general malaise along with the emotional discomfort of giving up a desired behavior. Those who progress to this stage in the course of dependence struggle repeatedly with attempts to cut down or control their opioid use. Some may even quit for a short time, suffering some level of withdrawal distress, and ironically, use this success to justify their denial of a problem. The relapse back to problematic opioid abuse is evidence that individuals are unable to sustain abstinence by their own force of willpower.

RELAPSE

Understanding relapse is key to understanding addiction, and the diagnostic feature of loss of control is central to the problem of relapse. During the weeks, months, and perhaps years of opioid abuse, individuals have resorted to opioid ingestion for pleasure or relief of discomfort. When the desire for pleasure or the need for stress relief arises, the tendency is for individuals naturally to resort to opioid use. The essence of loss of control is the inability to use opioids in moderation consistently. When persons return to opioid use, the inevitable struggle to manage it ensues. Unfortunately, the addicted brain is primed for this exposure and once joined, the battle is already lost.

FACTORS CAUSING INCREASED USE

Several factors have contributed to the spread of opioid addiction since the late 1980s. First, the purity of street heroin has increased while the price has declined. Analysis of street heroin seized by the U.S. Drug Enforcement Administration chronicles a

dramatic change in the street market for heroin. In 1980 the average purity of street heroin was less than 5 percent. By 1998 the average purity had risen to over 40 percent, and street level purity over 60 percent was not rare. Over the same time period the average price for a pure milligram of heroin dropped from about $4 to less than $1. This cheap and highly pure heroin made its way to rural areas where young experimenters were able to experience powerful opioid effects from intranasal use (snorting). The elimination of the need for intravenous injection and the use of needles made heroin easy and attractive to use. Eventually many of these became intravenous users as their tolerance increased along with their desire for more intense effects. The end result was extreme tolerance and physical dependence to high-dose intravenous heroin.

The second factor contributing to increased levels of youth exposure to opioids was a tremendous increase in the prescription of opioids for pain management. Some evidence points to the large-scale diversion of prescription opioids. Whether young people were buying prescription opioids from illegal street vendors or pilfering medication from their households, in 2004, about 20 percent of teens nationally had tried prescription opioids, second only in prevalence to the percentage who had tried marijuana and exceeding the percentage who had used inhalants. At the close of the twentieth century, the United States was facing a burgeoning problem of opioid addiction and a constraint on its ability to provide treatment for this condition.

RISK FACTORS

Social research has identified risk factors that make some individuals more vulnerable to addiction than others and protective factors that provide some measure of risk reduction. It has long been known that genetic influences are at work in alcoholism. Thus while the general population risk of alcoholism is about 13 percent, this rate increases to 50 percent for sons of alcoholic fathers. The role of genetics in the acquisition of opioid addiction is not clear, but there is good evidence from family studies that opioid dependence is familial. Further, three recent linkage studies of opioid dependence have identified regions of chromosomes that are likely to harbor genes that increase risk of opioid dependence. However in general, whereas poor social skills and early aggressive behavior are regarded as risk factors, positive relationships and self control are protective factors. Drug availability and lack of parental supervision increase vulnerability, whereas parental monitoring and support and anti-drug use policies in the school have the opposite effect. (Leshner, 1997, pp. 45–47).

THE ADDICTED BRAIN

Alan Leshner, past director of the National Institute on Drug Abuse (NIDA), wrote an article titled "Addiction Is a Brain Disease—and It Matters." In it he argues, on the basis of years of research studies and clinical reports, that the addicted brain functions differently from the non-addicted brain. He cites evidence for this conclusion, including the addict's behavioral and emotional reactions to visual, auditory, and olfactory stimuli that produce no reactions in the non-addicted individual. For instance, the smell of a burning match, the sight of a crack pipe, and the sound of crack cocaine being heated in the pipe spark visible brain changes in cocaine addicts but not in non-users.

Nora Volkow, the director of NIDA, conducted extensive brain imaging research demonstrating clearly that the addicted brain's response to stimuli is known to be associated with addicts' drug use behaviors. Thus, it is widely known as of 2008 that drug addiction has powerful physiological underpinnings that, once established, are terribly difficult to overcome. Every behavior associated with the procurement, preparation, and administration of one's drug of choice (in this case, opioids) is neurologically connected to the primitive reward circuitry of the brain. In the addict's brain, the use of opioids is hooked into the same survival circuitry that underlies other life sustaining behaviors such as eating, drinking, and sex.

The treatment of opioid dependence in the United States has a long and convoluted history, well described by David Musto in *The American Disease.* Modern treatment can draw on abstinence-oriented approaches that employ counseling, support group interventions, and medication therapy. The most powerful approach combines these elements into a comprehensive program of care and adds urine testing to identify episodes of drug use as another key element.

RECOVERY

Recovery from opioid dependence requires critical changes in one's thought processes as well as one's behavior. Change is difficult in any circumstance and is fraught with ambivalence. In the case of opioid dependence, the ambivalence is particularly powerful as the addict vacillates between the compulsion to use opioids and the need to quit.

The change process was described by researchers J. O. Prochaska and C. C. DiClemente (initially related to smoking cessation, but which has been applied to opioid dependence) using a model that identifies five stages (Prochaska et al., 1992). The first is *precontemplation* in which individuals are not considering making a change even when confronted by others. As their condition worsens, they may begin to feel that change would be good but are not ready to make a firm commitment to change. This second stage is called *contemplation*. Continued losses in the areas of interpersonal relations, productivity, self-esteem, and health make the desire for change more urgent, and addicts begin making concrete plans to change. During this third stage, called *preparation*, they may seek out information about treatment options, may consider the availability of medication therapy, and may make telephone calls to treatment programs or physicians who provide addiction services. When they enter the treatment system they have moved to the fourth stage of change called *action*. They begin to put into play the behaviors necessary to quit using opioids. The fifth stage is termed *maintenance*, which is perhaps the most difficult stage of change in that sustaining abstinence requires different thoughts, behaviors, and skills than does the initial act of quitting.

When abstinence is imposed abruptly, as in the case of incarceration, addicts have not had ample time to work through the psychological challenges that accompany the process of change. Thus, despite having achieved abstinence, relapse frequently occurs soon after release from detention. The same situation occurs when their treatment is imposed by an outside authority (e.g., parent, employer, court). Although abstinence can be sustained while the coercive forces are applied, unless the motivation for change is vigorously addressed in treatment and internalized by addicts, the likelihood of long-term recovery is low. Fortunately, for some individuals, the transition to self-motivated recovery does take place, and in such cases individuals entering treatment through coercion have good outcomes.

Paradoxically, the chronic progressive nature of addiction coupled with the psychological defense process called *denial* and the effects of almost constant drug intoxication makes spontaneous change unlikely. The tension between others recognizing the need for change and the addict who feels that change is unnecessary can reach an unbearable level. This predictable dynamic is the cause of much family strife whether the addict is a child, parent, or spouse.

TREATMENT OF ADDICTION AS A CHRONIC DISEASE

The importance of understanding addiction as a chronic disease applies not only to friends and family but also to the addict. The belief that opioid dependence is simply a drug problem leads many addicts on a desperate search to rid themselves of the drug as quickly as possible. If abstinence from illegal opioids is achieved without acknowledging the *brain disease* components of addiction, abstinence will be short lived. Staying engaged in treatment long enough to learn this information, absorb it, and assimilate it into one's life may be the most important factor in addiction treatment.

Medications have proven useful in opioid addiction treatment. Three prescription drugs approved by the U.S. Food and Drug Administration to treat opioid dependence are currently in use. They are methadone oral tablets and liquid, buprenorphine sublingual tablets, and naltrexone oral tablets. Methadone is perhaps the most well known of these medications. Its use for the treatment of opioid dependence is restricted by federal regulations to methadone programs. Methadone cannot be prescribed by private physicians for the purpose of opioid addiction treatment and can be legally obtained for this purpose exclusively through a licensed methadone program.

Buprenorphine (Suboxone, Subutex) can be prescribed by physicians who have completed at least a basic course in addiction medicine and are certified buprenorphine prescribers under the terms of the Drug Addiction Treatment Act passed by the U.S Congress in 2000. Federally authorized physicians for buprenorphine treatment can be found online. Buprenorphine prescriptions can be dispensed by

community pharmacies. One advantage of buprenorphine over methadone lies in its wider availability, especially relevant for opioid dependent individuals living in rural areas where methadone clinics are unavailable and the burden of travel is great. The unique pharmacology of buprenorphine makes it less likely to be abused by opioid addicts, especially in the naloxone-containing formulation called Suboxone.

The hurdle of opioid withdrawal distress is a barrier to abstinence for many opioid addicts. Both methadone (a full agonist) and buprenorphine (a partial agonist) activate opioid receptors and reverse the effects of opioid withdrawal. The immediate relief of withdrawal sickness is an attractive property of these agents. These medications make the entry into treatment less onerous by removing this stumbling block. Either of these medications can be effectively used in doses that first stabilize the patient's condition and then are tapered off, leaving the individual free of opioids at the conclusion of medication therapy. It has been said that "[w]ithdrawal services are essentially acute services with short-term outcomes, whereas heroin dependence is a chronic relapsing condition, and positive long-term outcomes are more often associated with longer participation in treatment" (Vorrath, 2001, p. 30). Engagement into treatment may be facilitated by medication therapy, but medications alone are insufficient intervention for the long-term management of the disease.

Maintenance treatment recognizes the limitation of medical withdrawal and employs the use of methadone or buprenorphine for months or years rather than days or weeks. The patient's physical dependence is sustained but since the medications are provided through legitimate channels in formulations that have low abuse potential and diminished reinforcing effects, the destructive elements of drug seeking behaviors are eliminated. A single daily dose of either medication produces a stable effect rather than the highs and lows of multiple daily doses of illicit opioids. This stabilizing effect on opioid physical dependence is one goal of maintenance therapy. Keeping patients attached to treatment services, including those that address disabilities that accompany, but are not central to, opioid dependence (e.g., family, social, educational, and general health problems) is another. Multiple studies have demonstrated the therapeutic benefit of maintenance treatment with both methadone (Ball & Ross, 1991) and buprenorphine on multiple dimensions of patients' lives. Reduced opioid abuse and other criminal activity, improved interpersonal relationships, increased employment, and better physical and mental health are some of the consistently measured beneficial outcomes of maintenance therapy.

While engaged in maintenance therapy, patients optimally are simultaneously immersed in recovery activities with the goals of changing the way they think and the way they act. Successful patients learn new ways of responding to the elements of daily life that were woven into their addiction. People entering recovery find that while they want to change, the world around them is essentially the same. They continue being exposed to the environments in which they bought and used opioids; friends with whom they shared drug experiences continue calling; negative emotions that prompted opioid use have not been resolved. Maintenance therapy keeps patients engaged in treatment long enough to deal with these challenges and provides a measure of protection against unplanned opioid ingestions.

Naltrexone (Trexan) is a medication that has effects opposite those of methadone and buprenorphine. Naltrexone is an opioid receptor antagonist (blocker) and offers no relief from withdrawal distress, but if taken regularly it prevents opioids from accessing and activating the body's opioid receptors. In doing so, naltrexone prevents opioid effects in the brain or other locations in the body. Whereas a person abusing opioids today can begin a course of treatment with methadone or buprenorphine tomorrow, one complication of naltrexone is that a person must be free of opioids for least seven to ten days prior to beginning its use, since it precipitates a severe withdrawal reaction in individuals who are physically dependent on opioids. Another weakness of naltrexone is the low rate of adherence among those for whom it is prescribed.

New science, better clinical techniques, and advances in medication therapy have made opioid addiction more clearly understood and more effectively treated. Continuing challenges in the United States revolve around attempts to prevent opioid

abuse through strategies that either reduce the demand for opioids or restrict their supply on the street. The creation of new scientific and clinical knowledge can lead to improved programs of intervention and treatment. Effective implementation of sound policies can limit availability of opioids and expand access to treatment. Together, these efforts will hasten the nation's efforts to respond effectively to the problem of opioid abuse and addiction in modern times.

See also **Addiction: Concepts and Definitions; Britain; Coerced Treatment for Substance Offenders; Conduct Disorder and Drug Use; Crime and Drugs; Opiates/Opioids; Opioid Complications and Withdrawal; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Wikler's Conditioning Theory of Drug Addiction.**

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OPIUM: INTERNATIONAL OVERVIEW.

Throughout recorded history, opiates have occupied a central place in medicine, renowned for their ability to relieve pain, cough, and diarrhea and induce a sense of well-being. Since the early twentieth century, they have symbolized the problems with attempts to control drug use through legislation and enforcement. From the days of the Silk Road to the present, opium has been an important commodity in world trade. (Technically, opiates are a subset of opioids, which also include synthetic agents and naturally occurring peptides that bind to opioid receptors in the brain.)

EARLY USE AND CULTIVATION

From about 2000 BCE, poppy cultivation spread throughout the Middle East, as evidenced by references to opium in inscriptions of ancient Sumer and Egypt. The physician Galen, in the second century CE, noted that opium cakes were widely sold in Rome. For many centuries, the opium poppy (*Papaver somniferum*) was grown in semi-arid parts of the Middle East and southern Asia, including dry or steep locales where other crops are difficult to cultivate. For traditional poppy farmers, opium was both a staple and cash crop that supplemented an agricultural livelihood. The entire plant was used: Poppy seeds were baked into breads; oil for cooking or fuel was extracted from them; and

the body of the plant was fed to cattle. The labor-intensiveness of collecting the opium-containing exudate from excised seed pods meant that whole families were pressed into service at harvest time. From this region, opium was transported to distant points where it was enjoyed or used as a medicine to relieve such symptoms as pain and diarrhea. It was a commodity in the transcontinental market that brought spices and silks from India and China westward; opium moved eastward and Muslim traders brought it to China in the eighth century.

During the Middle Ages, the severing of ties between Europe and the Middle East cut off opium shipments to Europe. In the Middle East, however, the ancient Roman and Greek texts remained important sources of knowledge. In these Muslim countries, where alcohol was forbidden, both opium and cannabis were widely used. In the thirteenth century Europeans rediscovered the old texts in Arabic translation; their translation back into Latin helped spark the Renaissance. Opium came to Europe at about the same time that Galen, who had systematized humoral theory in his second-century writings, became recognized as an important medical authority in Europe. Physicians interpreted opium's effect on bodily fluids (by promoting sweat or relieving diarrhea) as affecting humors. Galen's views were challenged by the sixteenth-century Swiss physician Paracelsus, who favored chemical remedies (such as mercury) to herbal ones. Nevertheless, Paracelsus valued opium; he mixed alcohol, opium, and other ingredients to make laudanum (from the Latin for "praise") to suggest its superiority. The English physician Thomas Sydenham wrote in 1680: "Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium."

An opium poppy. © EYE UBIQUITOUS/CORBIS.

TRADE AND INDUSTRIALIZATION

As Europeans discovered ocean routes to Pacific and Asian ports, beginning in the sixteenth century, goods that had traveled over the Silk Road were now loaded onto sailing ships that plied global trade routes in a market which increasingly involved drugs as commodities. The Dutch brought tobacco and introduced smoking to Asian populations in the sixteenth century. By the early seventeenth century smokers had begun adding opium to the tobacco; in time, opium was smoked by itself. This pattern of use was more social than medical, as men gathered to engage in the ritual of preparing the opium for smoking and together enjoying the languorous experience. Before long, some observers noted a pattern in which opium users steadily increased the amount they consumed and, if deprived of opium, exhibited symptoms of physiological and mental distress—what would later be called addiction. Concern about rising levels of use prompted the Chinese emperor to ban opium use in 1729; similarly, Southeast Asian countries banned the import and use of opium in the early nineteenth century. However, imports and use continued to rise.

In the eighteenth century the British became increasingly active in transoceanic trade, establishing the East India Company to manage trade in India. The British public expressed a persistent demand for Chinese products, especially tea, whereas the Chinese desired little in the way of imports from Great Britain, preferring payment in silver. The British sought to redress the resulting

trade imbalance. Through triangular trade, the British satisfied the domestic demand for tea and reduced the silver drain by selling opium produced in India to the Chinese. By the 1830s opium was the dominant trade item between these countries. The Chinese government viewed the rising opium imports with growing alarm. Between 1838 and 1842, and again between 1856 and 1860, China and Britain fought two Opium Wars. The victorious British quelled China's attempts to prohibit the importation of opium, which continued to be an important cash generator in British overseas trade until the late nineteenth century. Use in China became widespread as domestic production in addition to imported opium increased the availability of the drug, prices dropped, and its purchase came within reach of poorer groups. By the early twentieth century its use was widespread.

Britain also experienced growing demand for opium over the course of the eighteenth and nineteenth centuries. Persons seeking to treat themselves for various aches or ailments, or wanting to relieve drudgery, sleeplessness, or simply a persistent cough, could buy pellets of opium from apothecaries. This pattern persisted throughout most of the nineteenth century, although by the late eighteenth century physician Thomas Trotter had described the effect of chronic opium consumption: If a habitual user stopped taking the drug, a clearly recognizable syndrome of symptoms ensued. These included runny nose, sweating, aches, tremor, vomiting, and diarrhea. This phenomenon was seen to a large extent as the unfortunate consequence of taking medicines; it was not portrayed as a unique and devastating problem that threatened the social fabric.

Industrialization caused profound social shifts in England in the first half of the nineteenth century. People whose families had worked on the land for generations became part of the first large-scale factory workforce. Working conditions were brutal; men, women, and children worked 14-hour days, six days a week. Working women often had to bring young children to the factory with them. For working people, opium was an easily available source of relief for many complaints of both adults and children. The nonmedical use of opium spread among working classes in the United States and western European countries as they industrialized.

The incidence of addiction worried some observers, and this phenomenon became increasingly visible in part as a result of new pharmacological discoveries and changing medical technology. In 1806 Frederich Serturner of Hanover, Germany, announced that he had isolated the chief active component of opium, which he named morphine, after Morpheus, the Greek god of sleep. As the first drug compound to be isolated from the plant that contained it, this discovery launched scientific pharmacology. Drug effects could not be precisely described and measured until individual compounds were isolated. The isolation of codeine followed in 1832. In time, the systematic modification of the molecular structure of such compounds would be an important source of new medications and the basis of the modern pharmaceutical industry. Invention of the hypodermic syringe in the 1850s added a faster, more powerful route for delivering drugs such as morphine to the bloodstream and the brain. In 1898 the Bayer Company of Germany began marketing the newly trademarked heroin, produced by modification of the morphine molecule. Heroin was an early example of a product of pharmaceutical innovation that was initially valued for perceived therapeutic benefits (cough relief in this case) but whose psychoactive properties stimulated nonmedical use. As heroin quickly proved to be addictive, some observers worried that the pharmaceutical industry's ability to develop ever new medications might portend a profusion of new psychoactives whose use would cross medical boundaries into popular use.

Meanwhile, changing conditions in the late 19th century influenced the patterns and prevalence of opium use in Asia and Europe. As labor opportunities in China dwindled, Chinese men emigrated in search of work, taking the custom of smoking opium with them. They typically worked in grueling conditions, sometimes in environments where they were exposed to intestinal parasites and disease. Not only did opium provide solace at the end of a workday, it also relieved pain and diarrhea. In the British and American cities where Chinese immigrants formed Chinatowns, opium dens became fixtures in working-class neighborhoods, and English bohemians and American laborers began frequenting them. In both countries, troubling new patterns of nonmedical use of opiates further energized reformers, who characterized opium dens as lairs of alien vice. In the

United States, compassion for middle-class white women who became addicted to morphine after being introduced to it by their physicians shifted to alarm as young men in working-class neighborhoods began sniffing, then injecting, heroin. In such a framework, opiate addiction appeared as a scourge to be eradicated.

EFFORTS TO CONTROL

Reformers took an international as well as domestic perspective. From their efforts evolved the modern system of drug control. Protestant reformers and missionaries in Britain and the United States criticized both the immorality of the opium trade and disturbing patterns of use in their own nations and abroad. Starting in the 1880s, the British Society for the Suppression of the Opium Trade sought to end Britain's involvement in the opium trade. Physicians continued to be concerned about patients who became addicted to opium or morphine, their use often beginning for medical reasons.

An international treaty emerged from conferences held in Shanghai and the Hague between 1909 and 1914; it marked the beginning of coordinated efforts to control global opiate production. In the early 1920s the League of Nations created an Opium Advisory Committee to advance this work. Opium-producing countries and the European nations where (during this period) most of the world's opium was refined into drugs such as morphine or codeine also cooperated, agreeing to limit supplies of the drug. This supply-side approach to drug control has characterized the drug policies of most countries ever since.

On the domestic side, countries adopted varying approaches to opiate control. In the United States, the Harrison Narcotics Act of 1914 criminalized the use, possession, and sale of opiates. Following its implementation, a number of American cities opened clinics to treat addicts; it was unclear whether their purpose was only to help addicts through withdrawal or to allow them to take regular doses of opiates so as to maintain a controlled addiction and avoid withdrawal. The question soon became moot as the federal government, interpreting Harrison as not permitting addiction maintenance, closed the clinics. From the 1930s to the early 1970s, except for those who could afford treatment in private clinics, addiction treatment was available only through two federally run narcotic clinics that also functioned as prisons. Meanwhile, the federal government and local governments built an enforcement infrastructure intended to arrest, convict, and incarcerate users, buyers, and sellers of opiates; it grappled with a growing illicit market in heroin.

The British, seeking to avoid stimulating an illicit market, opted for medicalization. Physicians could prescribe opiates to selected addicts, maintaining their addiction. Opiate use continued to be associated with a small group of affluent bohemians and patients addicted through legally prescribed medication. In this context, nonpunitive policies appeared appropriate. China had legalized opium use at the end of the second Opium War. In the 1930s China was estimated to have 40 million opium users and opium production was widespread in the countryside. After World War II the Communist government enacted a sweeping policy of detoxifying addicts and quashing production; by the early 1950s opium use had been all but eradicated in the Peoples Republic. In Indochina, the French had begun licensing opium dens in 1870. Over the ensuing decades, several Southeast Asian countries maintained government opium monopolies, controlling production and garnering profits.

During the course of the twentieth century, diversity in policy gave way to a single model: criminalization. The United States took the lead in urging other countries to adopt tough punitive policies toward drug users and traffickers. After World War II the United Nations assumed the coordinating functions that had been exercised by the League of Nations' Opium Advisory Committee.

Enforcement structures and illicit markets grew in tandem, especially after World War II as heroin use increased significantly in the United States. As law enforcement succeeded in disrupting production or trade in one part of the world, the market would shift to another. In the early twentieth century, a time when heroin was still an officially approved medicine in many countries, most illicitly sold heroin was diverted from pharmaceutical factories in Europe. As the multinational effort to limit opiate production to medical needs gained strength, and as heroin lost favor as a medicine, traffickers took over the processing of opium into heroin.

Before World War II disrupted global heroin markets, most heroin flowing to Europe and the United States originated in Turkey, whereas heroin

production in Asia served intraregional markets. In the United States, the trade was managed by ethnic gangs that developed into alcohol-trafficking syndicates during Prohibition and shifted their attention to heroin following Repeal. Jewish gangs in the early twentieth century were succeeded by Sicilian gangs, which consolidated control over production, processing, and sales. After the war, Marseilles Corsicans' connections to Turkey and French Indochina made that city an important entrepôt for heroin smuggling. The United States persuaded Turkey to sharply curtail poppy production in the early 1970s; then, Southeast Asia became the world's leading producer. In the 1990s Afghanistan metamorphosed into the world's leading producer, with the insurgent Taliban encouraging production to finance its opposition to the Afghan government. Despite continuing international efforts to monitor the production and distribution of licit psychoactives, diversion from legitimate channels has persisted and contributed to rising levels of overdose.

On the demand side, the United States became the leading heroin-consuming country in the prosperous post-World War II era; while Congress enacted increasingly draconian punishments for drug trafficking, the drug issue simmered on a back burner in the national consciousness. Then, in the 1960s startling new patterns of drug use brought the issue to the mainstream in the United States and throughout Western Europe. Since the nineteenth century the leaders of American reform efforts aiming to curb drug use had couched their rhetoric as concern about use patterns among specific populations—foreigners or African Americans. In the 1960s many drug users were young, white, and middle-class. This new generation of drug users experimented with a range of drugs besides opiates.

Policymakers feared that rising levels of heroin addiction would fuel crime waves. As growing numbers of users developed dependence problems, the demand for treatment encouraged experimentation in new modalities (such as methadone maintenance) and expansion of treatment facilities (as in community-based residential or outpatient programs). The prevalence of stimulant use among the new generation of users challenged the prevailing definition of addiction, which had been based on opiates and other depressants. Rather than focusing on tolerance and a physiologically overt withdrawal syndrome, a new definition emphasized behavior and loss of control. In the United States, as treatment facilities expanded in both the public and private sectors, a medical approach to addiction has coexisted with the longer-standing system of enforcement and incarceration. Factors such as socioeconomic status and race have influenced which users entered which system. Destabilization following the fall of the Soviet Union contributed to rising levels of heroin use—and HIV infection—in the former Soviet republics.

OTHER IMPACTS

Opiates and their users have been refracted through various lenses. Romantic poet Samuel Coleridge exalted the dreamy state opium produced in his poem "Kublai Khan." His contemporary Thomas DeQuincey recounted his early infatuation with opium and later struggles to give up the drug in *Confessions of an English Opium Eater*. Eventually, heroin addiction came to symbolize addiction more generally and the heroin addict, especially in the United States, was cast as a junkie: a criminally involved male who symbolized profound deviance. Some heroin addicts embraced this outlaw status as a place from which to criticize conformism and hypocrisy in mainstream society; William Burroughs's novel *Junky* exemplifies this stance. Rock 'n' rollers of the 1960s celebrated heroin use, whereas punk rockers of the 1970s used heroin as a platform for challenging affluent societies in which deindustrialization had left them facing chronic unemployment.

Addictive drugs, led by the opiates, created opportunities for scientists studying the workings of the brain. Decades of pharmacological attempts to devise a nonaddicting opioid analgesic created a library of compounds that enabled researchers to hypothesize about brain function and contributed to the discovery of receptor sites in the brain for morphine and, later, other psychoactive drugs. The research field of neuroscience developed from the study of receptor sites and the role of molecules in communicating signals from one neuron to another.

The realization, soon after the first AIDS cases were diagnosed in 1981, that the mysterious new disease could be transmitted through shared syringes sparked new public health initiatives focusing on the

injectors of heroin and other drugs. The sense of emergency surrounding AIDS prompted activists in the Netherlands, Australia, Britain, the United States, and elsewhere to set up needle-exchange programs to distribute syringes to injectors and collect used ones for proper disposal. Working with active drug users challenged the assumption underlying most treatment modalities that abstinence (or stabilization on methadone) must precede any meaningful therapeutic engagement. However, needle-exchange activists discovered that their programs could engage participants in a range of services, including risk reduction education and referrals to drug treatment. From this work (and also from a public health approach to alcoholism) grew the philosophy of harm reduction. Rather than insisting that drug users must stop using drugs to receive other services, harm reduction values any behavioral change that reduces risk. Thus, using only sterile syringes, because it prevents the transmission of HIV, is a positive change even if the injection behavior continues. Initially controversial, in part because needle exchange was illegal where possession of syringes without a prescription was against the law, needle exchange has become increasingly—but not universally—accepted as an important public health measure to control the spread of infectious disease. In the early twenty-first century the development of harm reduction represents the latest significant change in policy approaches to dealing with the nonmedical use of opiates. Meanwhile, opiates remain important medications for the treatment of pain, cough, and diarrhea and critical tools for understanding the workings of the human brain.

See also **China; Golden Triangle as Drug Source; Harrison Narcotics Act of 1914.**

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OPIUM: U.S. OVERVIEW. Through much of American history, opiates have been central to an understanding of addiction, whether framed as a problem of medicine or public policy. From the Europeans' arrival to the late nineteenth century, opiates comprised one of the most important classes of medicines. In the 1900s, concerns about the nonmedical use of opiates shaped the development of American drug policy. In the late twentieth century, research on opiates provided a foundation for neuroscience, the study of brain function.

EARLY USES OF OPIUM

European settlers first brought opium to North America, where physicians administered it to relieve pain, cough, and diarrhea. A product of Asia, opium was a commodity in the shipping trade that connected the North American colonies with the rest of the world. As a medicine, opium was swallowed as pellets made from the exudate of the seed pods of the opium poppy (*Papaver somniferum*). Following the extraction of morphine and codeine from opium in the early nineteenth century, physicians relied more heavily on these compounds, though opium continued to be available for physicians to administer or patients to purchase.

In the first half of the nineteenth century, neither medications nor medical practice were regulated, and opiates were sold freely. During Andrew Jackson's presidency, the states repealed physician licensing requirements on the grounds that they created artificial elites. At the time, many people

treated themselves or their families with homemade or purchased remedies. Taking charge of one's own medical care reflected the broadened democratic spirit of the Jacksonian Age.

Physicians also administered opiates generously as part of the "heroic" brand of therapy. Based on humoral theory, "heroic therapy" interpreted disease as an imbalance of bodily fluids and sought to restore balance through the administration of drugs whose visible effects provided evidence of their efficacy. Whether by producing sweat or inhibiting diarrhea, opiates demonstrated their efficacy in regulating bodily fluids. Physicians also valued opiates for their wide-ranging ability to relieve symptoms, including coughing and insomnia. For chronically weak patients, opiates improved spirits and energy, and they were thus considered to have a stimulant effect (although they are now classed as depressants).

The chief value of opiates, however, lay in their ability to relieve pain. This effect was enhanced with the introduction of the hypodermic syringe in the 1850s. Some American physicians were quick to adopt the syringe, using it to inject morphine under the skin to treat painful local conditions such as facial neuralgia. They valued the faster and stronger onset of the drug's effects this method produced, compared to oral administration. Morphine remained one of the most commonly injected drugs over the rest of the nineteenth century, and it was administered for a lengthening list of conditions. During the American Civil War (1861–1865), the combination of the more potent morphine, the hypodermic syringe, and wartime conditions contributed to widespread hypodermic morphine use. Wounded soldiers were given syringes and supplies of morphine to treat their own pain, and some became addicted. Following the war, many of these soldiers phased out opiate use as their wounds healed, but others continued using morphine for years.

THE POST-BELLUM PERIOD

The late nineteenth century witnessed the rise of a burgeoning market in medications advertised to the public through increasingly sophisticated methods. Opiate-containing preparations were pitched for women's ailments, children's colic, teething pain, and other similar uses. Labels made extravagant claims but frequently obscured the contents of these products. Morphine, with its ability to ease pain and induce calm, was a common ingredient in such medications. Men, women, and children consumed opiates, often unknowingly, as a normal part of maintaining health and managing moods. Use was especially high in the South. All of these factors made the late nineteenth century the period with the highest rates of opiate use in American history.

The most common pattern of opiate use—and addiction—in the late nineteenth century involved white middle-class women who began taking morphine as medicine. Most were introduced to morphine by their physicians, but opiates were also available from pharmacies or mail-order houses. Some women took morphine to relieve menstrual cramps, and they taught their adolescent daughters to do the same. Others were treated for a medical condition and found that morphine induced a powerful sense of well-being. At a time when such women were expected not to drink alcohol (and thus were deprived of a socially acceptable form of drug use to modulate emotion or ease social anxieties), some found morphine to be a reliable means of banishing worry. When what began as episodic use became habitual, such women found themselves burdened with addiction. The character of Mary Tyrone in Eugene O'Neill's play *Long Day's Journey into Night*, which is set in 1912, exemplifies this pattern, in which addiction was a source of shame.

Addicts often sought treatment in privately run clinics that promised anonymity and offered little more than a place to rest while they went through withdrawal. Some addicts, meanwhile, purchased purported cures that merely contained more opiates. Others continued to take opium or morphine, managing their responsibilities as long as their drug supply remained uninterrupted. Medical and moral views combined to frame addiction as a tragic loss of self-control that all too often it resulted from a physician's liberality in prescribing morphine.

In the early 1890s, physicians began to express concerns about rising levels of addiction. Some studied addiction as a medical problem termed *inebriety*. They believed that addiction to alcohol and to opiates reflected the same disease process. Psychiatrists established inebriety hospitals, modeled on insane asylums, for the treatment of alcoholics and morphine addicts. Other physicians urged their colleagues to reduce the prescribing of opiates. These

concerns reflected the spirit of reform that was transforming medicine into an elite profession with epistemological foundations in the scientific laboratory. From this perspective, opiates' ability to relieve symptoms rather than attack the cause of disease cast them as old-fashioned. Addiction caused by a physician's actions tarnished the image these reformers sought for scientific medicine, and they urged that morphine use be restricted to a few conditions at minimal doses for short periods.

SHIFTING DEMOGRAPHICS OF USE

As industrialization, urbanization, and immigration transformed American society, new nonmedical patterns of opiate use arose. After 1850, Chinese laborers came to the American West to build the railroads and work at other forms of gang work. Some Chinese settled in Pacific coast cities, and they brought with them the practice of smoking opium to induce a two-to-three-hour state of dreamy relaxation. Whites, including laborers fearful of workplace competition, framed this practice as a sign of racial depravity. This racial linking, which demonized both a drug and its users, recurred repeatedly in the twentieth century.

From the 1880s until World War I, southern and eastern European immigrants came to America seeking jobs in the industrializing economy. They settled in crowded working-class neighborhoods in American cities, along with rural whites and, beginning in the early twentieth century, African Americans. The Americans who grew up in these neighborhoods encountered an emerging working-class entertainment scene that included dance and pool halls, brothels, and saloons. As young adults, they danced to early jazz, drank beer or whiskey, and sniffed cocaine or heroin. Bayer had introduced the latter drug in 1898 as a superior cough remedy, but thrill seekers found that crushing and sniffing the tablets produced a state of euphoria. Some of these users progressed to injecting heroin. The sale of both drugs remained unregulated, though some pharmacists exercised discretion in selling drugs. By 1910 the typical American opiate addict was a young man living and seeking amusement in a working-class neighborhood. Like the nineteenth-century matrons who injected morphine to relieve pain and assuage social anxieties, these men (and some women) used heroin from a mixture of motives: enjoyment with friends, relief of physical or emotional pain, and—when occasional use progressed to addiction—relief of withdrawal symptoms.

Heroin was a product of pharmaceutical research: A manipulation of the morphine molecule resulted in a semisynthetic compound whose effects were identical to those produced by morphine but came on faster and more intensely. As such, it exemplified an emerging trend in which pharmaceutical companies introduce new psychoactive compounds as medications. When users find them pleasurable, they incorporate them into nonmedical, social contexts of use.

THE PROGRESSIVE ERA AND EARLY LEGISLATION

By the early 1900s, opiates had become a physician's conundrum and a symbol of urban vice. Concerns about opiate addiction shifted from compassion for innocent victims of improper medication to fears of tough male heroin users. Physicians and Progressives responded with alarm and reform. Physicians worried about iatrogenic addiction and the unregulated sale of mislabeled, ineffective, or adulterated medicines. Progressives worried that opiate addiction undermined the middle-class virtues of thrift and hard work.

Concerns about adulteration, overdose, and addiction associated with an unregulated drug market became acute around 1900. In October 1905, *Collier's* magazine began publishing *The Great American Fraud*, Samuel Hopkins Adams's classic series of muckraking articles that excoriated the hawkers of ineffective or harmful medications. Adams singled out opiates, with their enslaving potential for addiction, as especially corrosive of civic virtue. His articles influenced passage of the 1906 Pure Food and Drug Act, the first federal legislation to regulate the sale of pharmaceuticals. Although it merely called for truth in labeling and proved difficult to enforce, the act foreshadowed the creation of the Food and Drug Administration.

Meanwhile, Progressive reformers responded to the new migration patterns with programs to assimilate immigrants to what they construed as "American ways." Motivated by concerns from airless tenements to wife-beating fueled by drinking sprees, they investigated deleterious conditions and recommended solutions. Alarm about high rates of syphilis and gonorrhea, which Progressive and medical observers linked to prostitutes, provoked a campaign to suppress prostitution. Cities appointed vice

commissions to study prostitution, and their investigators reported widespread use of heroin and cocaine among denizens of brothels, among patrons of saloons where prostitutes picked up customers, and in the larger urban amusement districts. These investigators had discovered the new pattern of young male opiate addiction, and the civic leaders they reported to expressed alarm at the prospect of widespread addiction to drugs that seemed to vitiate the work ethic. Thus, parallel to the push to prohibit the sale of alcohol (except for medical use), a movement arose calling for the eradication of this newly perceived drug problem. Northern Progressives were joined by white southerners who brandished tales of cocaine-crazed Negroes committing violent crimes under the influence of that drug.

In the early 1900s, some states and localities restricted the sale of opiates. Congress did not take immediate action, because the Constitution left the regulation of medical practice to the states. In addition, even if they were being used in nonmedical ways, opiates were fundamentally understood to be medicines whose proper use was perverted by heroin-sniffing pool players and the like. However, pressure from another direction brought the issue of drug control before Congress. Protestant missionaries working in Asia believed the opium use they witnessed there contributed to what they perceived as economic backwardness. Between 1909 and 1914, reformers from around the world met at Shanghai and The Hague to urge worldwide control of opiate supplies so as to prevent nonmedical uses of the drugs. Some countries signed a treaty that marked the first attempt to develop a coordinated international system for controlling worldwide opiate supplies. The U.S. representatives to these meetings were embarrassed by the lack of federal legislation in the United States to control access to opiates.

The Harrison Act. A lobbying effort to bring American legislation into line with the goals of the Hague resolutions, combined with rising domestic concern about nonmedical use of opiates, led to passage of the 1914 Harrison Narcotics Act, the first U.S. law to control who could buy a drug. The act banned the sale of opiates, cocaine, and some other drugs, except as authorized by a physician. The American Medical Association (AMA), sensitive to charges that the overprescribing of opiates was the chief cause of addiction, supported the legislation. The Harrison Act set the basic course in drug policy that the United States has followed ever since, in that it sought to eradicate the use of proscribed drugs by controlling their supply. Attempts to reduce demand rather than supply—either by treating addicts or preventing drug use—have received less support.

Following implementation of the Harrison Act, health authorities in several American cities worried that the sudden lack of opiate supplies for addicts would create personal distress and a public crisis. They therefore opened clinics to dispense opiates to addicts so that they would not go suddenly into withdrawal when legal supplies were cut off. In many cases, however, the mission of the clinics was unclear. Were patients expected to wean themselves from opiates, for example, or would some be permitted to maintain their addiction with opiates supplied through such clinics? The U.S. Treasury Department, charged with enforcing the Harrison Act, moved vigorously to prosecute physicians who overprescribed opiates, arguing in court that the law specifically disallowed addiction maintenance. In 1919 the Supreme Court ruled that the wording of the Harrison Act meant that physicians could only prescribe opiates to addicts as part of a short-term detoxification program. Again, the AMA agreed. Armed with this legal support, the Treasury Department continued its enforcement against the clinics, and by the mid-1920s had closed them all. With the closure of the clinics, and as physicians became increasingly reluctant to treat drug users, opiate addicts faced drastically reduced treatment options.

THE ILLICIT MARKET AND LAW ENFORCEMENT

Opiate addicts, now forced to seek drugs in a growing illicit market, also faced a rising risk of arrest as government at various jurisdictional levels built an enforcement infrastructure. At the federal level, the creation of the Federal Bureau of Narcotics in 1930, with Harry Anslinger (1892–1975) as its head, moved drug enforcement out of the Prohibition Unit that oversaw enforcement of the 1919 Volstead Act. Following the repeal of alcohol prohibition in 1933, the Federal Bureau of Narcotics continued to enforce the prohibition of

opiate use. Anslinger, a skillful administrator with a background in diplomatic service, oversaw American participation in the League of Nations' Opium Advisory Committee, which furthered the work on international control of opium supplies that had been initiated through the Hague Opium Treaty. On the domestic front, Anslinger managed an efficient team of nationwide enforcement officials. Believing that harsh and early punishment would be an effective deterrent, he supported increasingly severe punishments for drug offenders.

NEW RESEARCH INITIATIVES

Proponents of the Harrison Act had believed that cutting off opiate supplies would reduce the opiate problem to trivial levels, obviating the need for research. Earlier, the inebriety movement had led to a welter of research initiatives through the 1910s. While many of these efforts were inconclusive, a body of knowledge about drug effects, the nature of addiction, and treatment methods had accumulated. In the wake of drug and alcohol prohibition, such research was abandoned and what had been learned was quickly forgotten. However, new research initiatives emerged in the 1920s.

In 1923, as the problem of opiate addiction persisted into the era of Prohibition, the U.S. Public Health Service assigned psychiatrist Lawrence Kolb (1881–1972) to study opiate addiction. Kolb concluded that chronic addicts suffered from personality deficits that caused them to feel inordinate pleasure from opiates and thus become mired in addiction.

In the private sector, the Rockefeller-funded Bureau of Social Hygiene, founded to study prostitution, created a Committee on Drug Addictions in 1919 to study opiate use scientifically. Its work was linked through personal and professional connections to drug enforcement officials in Washington and representatives to the League of Nations' Opium Advisory Committee. The committee hired the physician Charles Terry, who had established an innovative morphine clinic in Jacksonville, Florida, to oversee its work. The committee set Terry to determining levels of opiate use in six American cities, in an effort to assess the legitimate medical need for opium imports to the United States. Rather than mailing out surveys, as previous investigators had done, Terry traveled to each city and interviewed physicians, pharmacists, and others knowledgeable about the sale and use of opiates. The results constituted the first systematic attempt to determine levels of opiate use in a community setting. Terry and Margaret Pellens incorporated these findings, an exhaustive survey of research on opiates, with recommendations for a clinical approach to managing addiction, in *The Opium Problem*, a 1928 publication that remains a classic. The committee also sponsored a search for a nonaddicting analgesic to replace morphine, on the grounds that eliminating medical need for morphine would make it possible to end opiate imports and eliminate nonmedical use.

These strands came together in the 1930s when the Public Health Service opened Narcotics Hospitals in Lexington, Kentucky, and Fort Worth, Texas. These institutions functioned as both hospitals and prisons where addicted federal prisoners, along with addicted probationers and voluntary admissions, underwent a therapeutic regimen intended to replace the bad habit of drug use with a regulated, wholesome routine. The Lexington hospital also housed the Addiction Research Center (ARC), which helped carry on the search for a nonaddicting opiate analgesic. A means of identifying addictiveness was necessary to determine whether the new analgesics being produced both by the Committee on Drug Addiction (now overseen by the National Research Council) and American and European pharmaceutical companies were, in fact, nonaddicting. Once an addictiveness assay was developed at the ARC, it became the world's clearinghouse for determining the addictiveness of new opioid compounds.

Meanwhile, as the cohort that had become addicted in the early years of the century aged and died, it was replaced by comparatively fewer new addicts. Thus, the "drug problem" faded to the background of public consciousness. The prevalence of addiction declined even further as World War II disrupted world heroin markets.

POSTWAR USAGE

Following World War II, heroin again flowed to the United States, mainly as Turkish opium refined and smuggled by Corsican gangs. Meanwhile, new populations and new patterns of entrenched and

isolating poverty in American cities meant that heroin users were increasingly likely to be African American or Hispanic. A diversion of pills from the medical marketplace, including opiates, barbiturates, and amphetamines, also diversified patterns of use. Over the course of the 1950s, the age of first-time drug users fell as teenagers increasingly sampled ways to get high. Nonetheless, most Americans thought of heroin addiction as an exotic phenomenon associated with a city world of jazz and beatniks.

In policy circles, however, the heroin addict posed a serious symbolic threat. In the early years of the Cold War, when politicians fanned Americans' fears of Soviet spies masquerading as loyal Americans, a deviant identity like heroin addiction, which could be hidden from view, seemed particularly menacing. In this environment, Harry Anslinger inaccurately framed Communist China as a source of imported heroin intended to destroy the American spirit. Congress responded with the 1951 Boggs Act and the 1956 Narcotic Control Act, which imposed new, harsher penalties for heroin possession and sales. The Boggs Act included the first mandatory minimum sentences, marking a pattern in which judicial discretion, which had characterized Progressive Era criminal justice reforms, was steadily eroded. Not all agreed with ceding the drug problem to the criminal justice system, however. In 1958 the American Bar Association and American Medical Association jointly issued a report calling for less punitive responses to drug offenses and a greater emphasis on medical approaches to treating addicts.

THE 1960S

In the 1960s, startling new patterns of drug use brought the issue to mainstream consciousness. Since the 19th century, American reformers aiming to curb drug use had couched their rhetoric as concern about use among specific groups, such as the Chinese or black street criminals. Now, however, drug users were typically young, white, and middle-class.

The dramatic events of the 1960s prompted a generation raised during the prosperous 1950s to question the relatively calm and affluent world they had grown up in. The civil rights movement; the assassinations of President John Kennedy, Martin Luther King Jr., and presidential candidate Robert Kennedy; and the escalating War in Vietnam all had a profound effect on the youth culture of the 1960s. As they questioned adult authority, young people disregarded prohibitionist messages about illicit drugs. While they sought to forge new values, they also hoped to eliminate superficial and hypocritical aspects of American life. Marijuana and psychedelic drugs most closely symbolized the new spirit, but young people buying drugs on the illicit market and sharing lore about highs also encountered amphetamines and opiates.

In response to these trends, President Richard Nixon initiated the most significant changes in American drug policy since the passage of the Harrison Narcotic Act in 1914. The first legislative achievement was passage of the 1970 Controlled Substance Act, which established five schedules for ranking psychoactive drugs according to abuse potential and medical usefulness. When he became aware of a promising and inexpensive new treatment for heroin addiction, Nixon believed that it might reduce levels of heroin use and thus reduce crime levels as well. Beginning in 1963 in New York, Vincent Dole (1913–2006) and Marie Nyswander (1919–1986) had demonstrated that long-time heroin users, when stabilized on daily doses of oral methadone and supported with rehabilitative services, showed reduced criminal activity and improved functioning in social and employment areas. Nixon believed that methadone maintenance would provide a cost-effective means of reducing money-seeking crimes committed by street addicts. In 1972 he proposed, and Congress created, the National Institute on Drug Abuse (NIDA) to fund community-based drug treatment and coordinate research. The latter included studies of drug effects in the brain and contributed to the emerging field of neuroscience. Other inpatient and outpatient treatment modalities joined methadone maintenance as community-level resources for addicts. On the enforcement side, a new Drug Enforcement Administration replaced earlier agencies.

In addition, NIDA funded ethnographic studies of drug using. Inspired by the work of the sociologists Alfred Lindesmith (1905–1991) in the 1930s and Howard Becker (b. 1928) in the 1960s, as well as the work of sociologists at the Addiction Research Center at Lexington, a

generation of ethnographers provided insights into social influences on drug-using behavior. Among the important studies done at this time was Lee Robins's work with Vietnam veterans. Robins (b. 1922) concluded that most veterans did not resume heroin use when they returned to their home communities.

NEW TREATMENT MODALITIES AND HARSHER PENALTIES

In the 1970s, under federal leadership, treatment programs were expanded and new ones created in cities across the nation. Increasingly, those running the programs encountered patients who did not fit the model of the criminally involved long-time heroin addict. Younger patients, women, and those using a variety of drugs reflected changing U.S. drug-use patterns, and opiates became just one group among many psychoactive drugs that were traded on the illicit market and used for recreational, lifestyle, political, or habitual reasons. As these other drugs (particularly cocaine) grabbed headlines, and as Americans' concerns focused on drug use by children as young as twelve, the national mood swung back in favor of harsh punishments for drug use. First Lady Nancy Reagan captured this mood with the slogan "Just Say No," and during Ronald Reagan's two terms as president, Congress again stiffened penalties for drug use and trafficking.

HIV, Drug Use, and Harm Reduction. Even as federal policy hardened, the advent of AIDS and the recognition of injection drug users among its earliest victims created opportunities for new public health perspectives on drug use. In the politicized context of AIDS, with its advocacy of patient activism, drug users and public health researchers directly addressed this risk. In the late 1980s, activists in a number of American cities began distributing sterile syringes to injectors to obviate the need for sharing, and thus prevent transmission of HIV. Studies established that these needle-exchange programs effectively deterred HIV transmission without increasing drug use. Over the ensuing years, localities and states used public health authority or changed laws to allow needle-exchange programs to operate with legal sanction. Needle exchange was a foundational policy initiative in the emerging movement of harm reduction.

As the possibility of HIV infection through sharing syringes became widely recognized, first-time heroin users increasingly sniffed the drug to avoid this risk. The market responded with a more potent form of heroin that was suitable for smoking. Nonetheless, many sniffers, as their tolerance rose, switched to injecting. In response to higher potency of heroin on the illicit market and the diversion of licit pharmaceuticals, such as a time-release formulation of oxycodone, overdose deaths rose dramatically. In response, harm reduction programs began overdose prevention trainings and distribution of naloxone, an opioid antagonist that reverses opioid overdoses.

In the harm reduction movement, unlike earlier initiatives to address drug problems, drug users were active in a public health movement addressing their own interests. But these initiatives faced opposition. Some treatment professionals believed that working in any way with drug users without engaging them in treatment for their drug dependence was counterproductive. Many of these individuals changed their minds as they saw the value of helping users avoid life-threatening disease until they became ready for treatment. Others, however, have opposed needle exchange on political grounds, viewing it as inconsistent with the overarching goal of federal drug policy to eradicate the nonmedical use of opiates and other illegal drugs. Still others have supported prohibition while arguing that reduction in drug-related harms constitutes a better measure of policy success than a reduction in the amounts of drugs used or numbers of users. While these debates continue, federal policy has remained committed to enforcement, with a lesser emphasis on treatment and prevention, and opposed to needle exchange and harm reduction.

See also **Foreign Policy and Drugs, United States; Harm Reduction; Harrison Narcotics Act of 1914; Opiates/Opioids; Opium: International Overview; World Health Organization Expert Committee on Drug Dependence.**

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OVERDOSE, DRUG (OD). Administration of a drug in a quantity that exceeds that which the body can metabolize or excrete before toxicity develops constitutes an overdose. Whether it is accidental or deliberate, drug overdose is a significant problem encountered by providers of emergency medical care. Accidental overdose is common among users of illegal substances of abuse, since little reliability can be placed on the potency, presence of adulterants, and even identity of the street substance. For example, heroin potency has been demonstrated to range from 3 to 90 percent. Overdoses and deaths from heroin are therefore common. The prevalence of comorbid disorders, particularly depression, in substance-abusing populations, has been found to be high. Thus, deliberate drug overdoses taken in the attempt to commit suicide are frequently encountered in this population. Also, people with a psychiatric illness but no drug-abuse problem most often attempt suicide with a drug overdose. Substances frequently implicated in drug overdose involve nonnarcotic analgesics (painkillers), benzodiazepines (tranquilizers), opiates, or antidepressants—often in combination with alcohol.

The treatment of a drug overdose begins by providing basic supportive care (i.e., ensuring that there is adequate ventilation and monitoring the heart), calling 911, an emergency medical service (EMS), or the Poison Control Center (see Appendix I in Volume 4). If little time has elapsed since ingestion, efforts may be made to prevent further absorption of the drug by such means as gastric lavage or by administration of activated charcoal. Other treatments include increasing the rate of excretion through forced diuresis or giving specific antidotes (e.g., naloxone for opiate overdose) when the substance is known or can be identified from the presenting clinical syndrome. Obtaining a careful drug history from the patient or accompanying individuals is of paramount importance in effectively treating and minimizing risks from a drug overdose, which often results in death.

See also **Drug Abuse Warning Network (DAWN); Drug Interactions and Alcohol.**

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OVEREATING AND OTHER EXCESSIVE BEHAVIORS. Overeating is grouped together with substance abuse and dependence in a large group of disorders designated as behavioral (non-substance-related) addictions. The term *impulse control disorders* has been used by some clinicians to describe these behaviors. In this context the notion of *addiction* centers on the repetitiveness of the behavior and would include such behaviors as compulsive spending, compulsive gambling, excessive computer gaming, pathological overeating (bulimia), hypersexuality, kleptomania (repetitive, compulsive stealing when there is no need), as well as such miscellaneous obsessive-compulsive behaviors as tics and hair-pulling (trichotillomania).

Research into the neurobiology of these behaviors as of 2008 is in an early stage. Advances in understanding motivation, reward, and addiction have provided insight into the possible pathophysiology of these disorders. Some researchers have pointed out similarities among these disorders and speculate that there may be similar brain mechanisms involved in some of them. For example, it has been shown that dopamine levels in certain areas of the brain (such as the nucleus accumbens) are elevated by the smoking of reinforcing drugs, including cocaine, amphetamines, opioids, marijuana, and, to some degree, nicotine. However, increased dopamine levels in these same brain circuits have been shown to occur when animals anticipate food or sexual activity. Also, learning, conditioning, and reinforcement play important roles in these repetitive behavior disorders as well as in the more traditional chemical or substance abuse and dependence disorders. It has also been pointed out that treatments for nonchemical addictive disorders often follow principles used in substance use disorders; for example, identifying trigger and high-risk situations, teaching alternative coping behaviors, and emphasizing relapse prevention. Self-help groups using principles of Alcoholics Anonymous have also been organized, such as Overeaters Anonymous or Gamblers Anonymous. Some pharmacologic agents appear to alter both drug ingestion and obsessive-compulsive behaviors that are not drug-related. For example, selective serotonin reuptake inhibitors, used as antidepressant and antianxiety medications, seem to help some alcoholics decrease alcohol consumption and compulsive hair-pullers reduce that behavior.

Such broad definitions of addictive behaviors have disadvantages when they focus too much attention on the commonalities among the diverse behaviors while minimizing the differences and particularities. At a time when rapid progress is occurring in the understanding of the biological processes associated with substance dependence, focusing only on commonalities may obscure the value of therapeutic interventions aimed at specific disorders. For example, nicotine transdermal patches seem to have considerable value in treating tobacco dependence but are probably of no value for cocaine dependence or compulsive gambling.

The way society (or science) chooses to categorize behaviors—desirable or undesirable, repetitive or episodic—is determined in large measure by the objectives of developing the categorization. There are probably some circumstances in which it is helpful to think about a broad category of problematic excessive behaviors encompassing everything from substance abuse to excessive Internet gaming. There is also the risk that in doing so researchers convey the notion that excessive drug use is no more serious or refractory to intervention than Internet gaming. Certainly in the early twenty-first century, the social costs and medical consequences of the substance use disorders are so great that researchers should be cautious about embracing any conceptual scheme that tends to trivialize or make these problems seem less serious than they are.

See also **Addiction: Concepts and Definitions; Obesity; Research, Animal Model: An Overview; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Risk Factors for Substance Use, Abuse, and Dependence: Learning.**

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OVER-THE-COUNTER (OTC) MEDICATION. This class of medication can be purchased without a prescription. Which medications require prescriptions and which do not varies widely from country to country. Common examples of OTC medications in the United States include analgesics (aspirin, Tylenol), cough and cold products (Sinutab, Drixoral), allergy medications (Benadryl, Tavist), gastrointestinal products (Maalox), antidiarrheals (Imodium), and nicotine replacements (e.g., Nicorette gum, Nicoderm patch). Recently, a number of medications that previously were sold only by prescription have been made available over the counter. These include medications that block the production of gastric acid to relieve heartburn (Axid AR, Tagamet HB 200, Zantac 75) and nicotine gum (Nicorette CQ) and the nicotine patch (Nicotrol, Nicoderm CQ) for smoking cessation.

Prescription medications are labeled with patient-specific instructions determined by a physician whereas OTC products provide general information for use by consumers. OTC products *are drugs*, and as such they may cause side effects or adverse effects; or they may interact adversely with foods, alcohol, or other medications. Some of the more than 500,000 OTC products that are available have the potential to be misused or abused. Antihistamines, hypnotics, decongestants, analgesics, laxatives, and diet pills are often consumed in higher than recommended quantities; they have caused physical and/or psychological dependence. An epidemic of the early 1990s among adolescents has been "baby speed," the combining of OTC caffeine pills with the decongestant pills pseudoephedrine. Handfuls of these pills cost only a few dollars and are responsible for overstimulating the heart and central nervous system, causing strokes and death.

An estimated 28 percent of adults in the United States use all kinds of OTC products, often responsibly but also in combination with prescription medications or alcohol. The high cost of visits to a physician and stays in a hospital has generated heightened interest in self-medication, which has increased opportunities for pharmacists to counsel patients. This situation is also contributing to the increased availability of medications as products are transferred from prescription to OTC status. The legislation that controls OTC products is quite recent. It was in 1951 that the United States first separated drugs into the two categories—prescription and OTC. A drug that is available only on prescription cannot be made available as an OTC product until its relative safety and efficacy have been reviewed by the U.S. Food and Drug Administration (FDA).

See also **Drug Interactions and Alcohol; Legal Regulation of Drugs and Alcohol.**

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OXYCODONE. Oxycodone is one of the most widely used opioid analgesics in the United States, and it is usually used in conjunction with the analgesics aspirin or acetaminophen. The combinations have proven effective and are in some ways superior to oxycodone alone, since they permit a lower dose of the opioid. They are therefore less likely to produce constipation, drowsiness, and nausea. Oxycodone is a derivative of oxymorphone, the relationship being the same as that between codeine and morphine. Like codeine, oxycodone is metabolized to oxymorphone, which is assumed to be responsible for its activity. Pharmacologically, the actions of oxycodone and oxymorphone are quite similar to those of morphine, so toxicity and addiction can occur. The availability of slow-release formulations (Oxycontin), containing larger quantities of the drug in each pill, has contributed to major problems with its diversion and abuse.

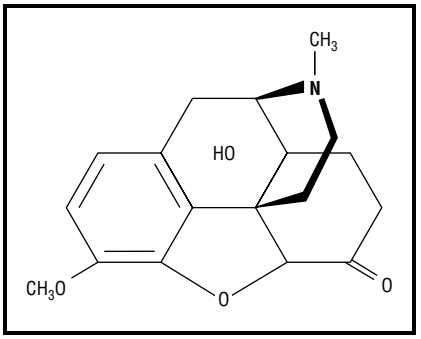

Figure 1. Chemical structure of oxycodone. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Opiates/Opioids; Opioid Complications and Withdrawal; Opioid Dependence: Course of the Disorder Over Time; Oxymorphone.**

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GAVRIL W. PASTERNAK

OXYCONTIN. Prescription opioids, including oxycodone (OxyContin), are among the most commonly misused types of prescription drugs. OxyContin and Vicodin are the most frequently named pain relievers causing visits to hospital emergency rooms, being involved in 40 percent of such visits. OxyContin and Vicodin are more commonly associated with polydrug use than any other drugs. Approximately 75 percent of emergency room visits involving OxyContin and Vicodin also involve other drugs, such as alcohol and benzodiazepines, whereas approximately 50 percent of all drug abuse-related visits involve multiple drugs.

Of all opioids used nonmedically, OxyContin has raised the most concern among communities, researchers, and physicians for its abuse potential. OxyContin—also known as Oxy, killer, and hillbilly heroin—differs from other pain medication in that it contains a much larger amount of the active ingredient oxycodone. OxyContin is legally prescribed as a timed-release tablet, providing as many as 12 hours of relief from chronic pain. Abusers crush the tablet to disarm its timed-release action, which results in a quick, powerful high that has been compared to the euphoria associated with heroin. Once the tablet is crushed, the drug is administered by one of three methods: orally by swallowing; intranasally by sniffing; or intravenously after mixing it with water. Like other drugs that are administered intranasally or intravenously, OxyContin places users at risk for bloodborne pathogens such as hepatitis or HIV, as well as for overdose. Because its effects mimic heroin, an active black market has developed around OxyContin. A 40-milligram pill costs approximately US $4 by prescription, yet it may sell for $20 to $40 on the street. OxyContin is of particular concern because of its potency and its association with misuse, which could result in dependence, overdose, or death.

See also **Epidemics of Drug Abuse in the United States; Prescription Drug Abuse.**

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OXYMORPHONE. Oxymorphone is a potent semisynthetic opioid analgesic derived from thebaine, one of the twenty alkaloids occurring naturally in opium. Oxymorphone is approximately fivefold more potent than morphine and has very similar actions and side effects. It is used to treat moderate to severe pain. Oral formulations are not available in the United States, but it is available by injection or by rectal suppository. Like morphine, continued use of oxymorphone leads to tolerance and physical dependence. It is interesting that oxymorphone shares the same basic chemical structure

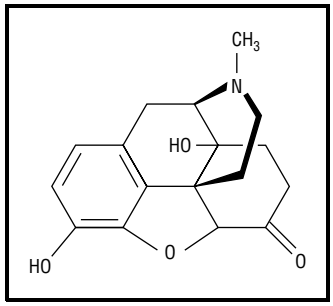

Figure 1. Chemical structure of oxymorphone. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

as the antagonists naloxone and naltrexone, the only difference being the substituent on the nitrogen. Neither naloxone nor naltrexone have analgesic activity; in contrast to oxymorphone, they are instead capable of blocking opiate actions.

See also **Alkaloids; Morphine; Naloxone; Opiates/Opioids; Pain, Drugs Used for; Tolerance and Physical Dependence.**

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PAIN: BEHAVIORAL METHODS FOR MEASURING ANALGESIC EFFECTS OF DRUGS. Pain is a sensation produced by such potentially harmful stimuli as intense heat, stretching, cutting, or chemical irritation. The ways in which information about these stimuli is carried to the brain and the interpretation that results are very complex. Pain sometimes occurs in the absence of a harmful stimulus, such as in phantom limb pain (where the limb has long been missing). In other instances, pain is not even felt, although harmful stimuli are present. Thus pain is both a sensation and a response to that sensation. The response to pain can vary depending on the individual and the circumstances. Given this complexity, it is not surprising that pain can be modified in many ways—by a variety of drugs, by hypnosis, and by such stimulation as acupuncture.

PAIN TRANSMISSION

The transmission of pain involves two systems—an ascending and a descending neural system. Ascending neural systems carry information about potentially harmful stimuli from peripheral nerves to the spinal cord and from there to the brain, where information about the emotional and psychological aspects of painful stimuli is incorporated. In addition, the perception of painful stimuli is altered by descending neural systems, which send information from the brain back to the spinal cord. Pain transmission can be altered at any point in this loop. Drugs such as aspirin (an analgesic) relieve pain by reducing pain sensitivity in the periphery. Local anesthetics such as lidocaine (Xylocaine) and procaine (Novocaine) relieve pain by blocking nerve conduction in specific areas. Morphine and other opioids (narcotics) alter pain transmission by interfering with the processing of painful stimuli in the spinal cord and the brain.

MORPHINE AND OTHER OPIOIDS IN HUMAN PATIENTS

Among all the drugs that relieve pain, opium and its derivative morphine, are certainly the best known. When morphine is given to patients who are experiencing severe pain, they often say the pain is less intense or that it no longer exists. Other patients say the pain is still present, but it just does not bother them. Thus, morphine affects both the sensation of pain and the patient's response to the painful stimulus. It is generally believed that morphine acts on both the spinal cord and the brain. In the spinal cord, morphine inhibits the flow of information about painful stimuli from the spinal cord to the brain. In the brain, morphine alters pain perception by modifying activity in the descending pain-control system. In addition to relieving pain, morphine-like drugs produce a sense of pleasure (or euphoria) in some patients. Morphine and other opioids are the most effective drugs known for the relief of pain. Although their usefulness is sometimes limited by the fact that they can produce dependence, this factor is generally not a problem in clinical settings.

NONOPIOID ANALGESICS

Although the opioids are considered the most effective drugs for the treatment of pain, THC

(delta-9-tetrahydrocannabinol), the active constituent of marijuana, has some pain-relieving properties, but it is not as effective as morphine in this respect. Very large doses of such drugs as alcohol and the barbiturates also appear to relieve pain; however, these effects do not represent true analgesia, since they occur only at doses of alcohol and the barbiturates that produce a loss of consciousness. Thus, the organism's lack of response to painful stimuli is simply an inability to respond.

STUDIES IN LABORATORY ANIMALS

To determine whether a newly-developed compound has pain-relieving properties, scientists use behavioral procedures developed in laboratory animals. In general, these procedures measure the time it takes an organism to respond to a painful stimulus, first when no drug is present and then after a drug is given. Morphine and other opioids consistently alter this and other measures of pain perception. For example, morphine increases the time it takes an animal to remove its tail from a warm water bath. It takes about 2 seconds for the monkey to remove its tail from a warm water bath if morphine is not given. A small amount of morphine increases tail-removal time to about 8 seconds; larger amounts of morphine increase the time to as much as 20 seconds. Modification of pain perception also depends on the intensity of the painful stimulus. If the water in the bath is very hot, only very large amounts of morphine will increase the time it takes animals to withdraw their tail, whereas a lesser amount of morphine will increase response time at lower temperatures. Similarly, some drugs such as buprenorphine are most effective in relieving pain when the pain is mild. Since buprenorphine also produces less dependence than morphine, it may be a very useful drug for treating mild forms of pain. By combining data about the pain-relieving effects of a drug with data about its likelihood of producing dependence, information is obtained about the usefulness of a new drug in a clinical setting.

See also **Addiction: Concepts and Definitions; Opiates/Opioids; Pain, Drugs Used for.**

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PAIN, DRUGS USED FOR.

Pain is a sensation unique to an individual. Its perception depends on the injury or condition involved and the situation or context. A bruise obtained in a football game may not be appreciated at the time of the injury, yet in other circumstances the pain from a minor injury, such as stubbing a toe, may be overwhelming. The extent of the injury does not predict the amount of pain experienced, and it is this wide variability that makes the treatment of pain difficult.

Within the brain, there are two systems that can appreciate the sensation of pain. One deals with the objective component and tells the exact location of the injury and what type of injury it is. The other is more diffuse and comprises the subjective sense of hurting. Many people have experienced both types of pain. Touching a hot object or stubbing a toe is quickly followed by the appreciation that an injury has occurred, followed an instant later by the pain. It is this second pain that contains the *suffering*, the *hurt*, and the elimination of this second pain is the goal of analgesic therapy.

THREE CATEGORIES OF PAIN

Physicians have divided pains into three general categories. The first, and most common, *somatic pain*, results from tissue injury, such as a broken leg, metastases in the bone from cancer, muscle pulls, or ligament sprains. The second, *visceral pain*, results from activation of pain fibers in internal organs, typically in the abdomen or chest. This category includes discomfort associated, for example, with gall bladder disease, peptic ulcers, or pancreatitis. Unlike somatic pain, visceral pain is poorly localized. The most difficult pain to understand and to treat is *deafferentation*, or *neuropathic pain*, which is a consequence of injury to nerves. It is difficult for patients to describe these sensations,

but they often use terms such as *burning*, *shooting*, or *electric*-like. This type of pain is commonly seen in cancer patients when tumors invade nerve bundles. It also is seen with mild damage to nerves.

The most common class of injury is the *peripheral neuropathies*. These disorders result from a wide variety of causes; they affect nerves as they course through the body. The longest nerves are most sensitive to injury, which explains why this type of pain is most likely to develop in the feet. Diabetes is one of the most common causes of neuropathy. A special type of pain also in this classification is *postherpetic neuralgia*, a burning and/or shooting pain associated with herpes zoster, known as *shingles*.

ACUTE AND CHRONIC PAIN

Pain can be classified as either acute (short-term) or chronic (long-term). The duration of many kinds of pain can be anticipated. The acute pain associated with surgery is usually limited in duration and, over the period of several days, decreases markedly. Chronic pain, by contrast, is usually defined as pain that persists for six months or longer. There are two types of chronic pain: malignant and nonmalignant. Malignant pain is that caused by cancer. Chronic nonmalignant pain conditions include but are not limited to musculoskeletal pain, osteoarthritis, fibromyalgia (chronic widespread muscular aching, and heightened sensitivity and needle-like tingling of the skin), headache, sciatica (leg pain caused by compression or trauma of the sciatic nerve), and complex regional pain syndrome (characterized by severe burning pain and swelling and changes in the skin). Despite the sophistication of modern medicine, some types of chronic nonmalignant pain are difficult to classify, diagnose, or treat. In some cases, chronic pain may seem to have no cause. In many cases, patients need to see specialists who have received specific training and are board-certified in pain medicine.

GROUPS OF PAIN MEDICINES

Pain medicines (analgesics) are often divided into three major groups. The first group comprises the most commonly used drugs, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). The second group includes the opioids (opiates). Some opioids are used for moderate pain whereas others are typically employed for more severe pain. Third, there are a number of drugs used either for specific pain syndromes or in conjunction with the first two groups. These agents, *adjuvant drugs*, include anticonvulsants (for neuropathic pain) and muscle relaxants (for back pain). The adjuvants are not discussed in this section because although they play a role in the treatment of pain, they are not considered as prototypic analgesics.

Table 1 lists different analgesics that are approved by the U.S. Food and Drug Administration as of 2008. They are divided into two major categories: non-opioids and opioids. Table 1 also provides typically recommended doses for acute pain (with two exceptions as noted) as well as frequency of dosing. The choice of analgesic is based on both the type of pain and its intensity.

Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Acetaminophen. Most pain is treated in a standardized fashion. Initial therapy often utilizes acetaminophen and the NSAIDs, aspirin, ibuprofen, and naproxen. These nonopioid agents are available without prescription (i.e., over-the-counter, OTC) and can be very effective for mild to moderate types of pain. They have a number of properties that make them excellent analgesics. They all reduce fever and pain caused by muscle aches, the common cold, toothaches, menstrual cramps, and headaches. They also reduce pain caused by arthritis that is minor in nature. With the exception of acetaminophen, they also reduce inflammation. Their effectiveness against a wide variety of different types of pain and their oral dosage greatly enhance their utility.

Unfortunately, these OTC agents exhibit relatively low ceiling effects, which means that the maximal degree of analgesia that can be obtained by a drug can be limited, regardless of the dose. Several NSAIDs are only available by prescription and have greater analgesic potencies. Besides the prescribed NSAIDs listed in Table 1, others include fenoprofen (Nalfon), diflusanil (Dolobid), and piroxicam (Feldene). Primary indications for the prescribed NSAIDs include treatment of pain, tenderness, and swelling caused by rheumatoid arthritis, osteoarthritis, and other musculoskeletal ailments.

Typically, NSAIDs act at the site of injury, leading to their classification as peripherally acting drugs

as opposed to centrally acting drugs, such as the opioids, which work within the brain and spinal cord. The analgesic and anti-inflammatory effects of NSAIDs are achieved through the inhibition of the cyclooxygenase (COX) enzyme. The COX enzyme converts arachidonic acid to cyclic prostanoids (e.g., prostaglandins, thromboxane). There are two forms of COX: COX-1 and COX-2. COX-1 is expressed in nearly all tissues and is responsible for platelet aggregation (thromboxane) and protection of the gastrointestinal mucosa (prostaglandins). COX-2, by contrast, is released in response to tissue injury and produces pain and inflammation. Nearly all NSAIDs are termed nonselective because they inhibit both forms of the COX enzyme. The analgesic and anti-inflammatory properties of NSAIDs are achieved through inhibition of COX-2, whereas undesired side effects in the gastrointestinal tract and kidneys (discussed below) are produced through the inhibition of COX-1. In 1999, the first NSAID to selectively inhibit COX-2 became available in the United States; COX-2 inhibitors selectively block the synthesis of the prostaglandins that produce inflammation and pain, while allowing for the synthesis of prostaglandins that protect the gastrointestinal tract.

All NSAIDs carry risks. With the exception of aspirin, both nonselective NSAIDs and selective COX-2 inhibiting NSAIDs may increase the chance of a heart attack or stroke. These risks increase with longer use, higher doses, and in people who have a history of heart disease. Unlike other NSAIDs, aspirin actually reduces the chance of heart attack and stroke by decreasing the production of thromboxane through the selective irreversible inhibition of COX-1. Another risk is gastrointestinal insult (e.g., gastric ulcers, bleeding). Therefore, aspirin and other nonselective NSAIDs should be avoided in patients with ulcer disease. Studies have demonstrated that the incidence of gastric ulcers is lower in patients who use selective COX-2 inhibitors than in patients who use nonselective NSAIDs, but the evidence is less convincing that non-ulcer gastrointestinal symptoms such as dyspepsia (chronic or recurrent pain or discomfort centered in the upper abdomen) are associated with less risk. As of 2008, there was only one FDA-approved COX-2 inhibitor available in the United States: celecoxib (Celebrex). In 2004, the manufacturers of a then widely prescribed COX-2 inhibitor, rofecoxib (Vioxx), withdrew their drug from the market. The drug was associated with increased risk of heart attack and stroke associated with long-term, high dose use. Shortly thereafter in 2005, the FDA requested that the manufacturer of valdecoxib (Bextra) withdraw it from the market, due to its potential increased risk for serious cardiovascular adverse events and risk for serious skin reactions. Aspirin and other NSAIDs are also capable of producing renal (kidney) side effects, such as reductions in filtration rates.

Acetaminophen, the only non-opioid analgesic in Table 1 that is not an NSAID, does not irritate the gastrointestinal tract or produce renal side effects; however, it has its own potential problems. Although it is one of the safest drugs available when used as directed, overdoses with acetaminophen can be very dangerous, being associated with major damage to the liver, which can be life-threatening. Care must be taken to use only the recommended doses of acetaminophen.

Opioids. Opioids work within the brain and spinal cord to relieve the second pain—the hurt—described above. In this regard, they are highly effective since they take away pain without interfering with other sensations, unlike local anesthetics. It is this ability to selectively act on the hurt that makes them so valuable. There are a number of opioids that are used for the treatment of moderate to severe pain (see Table 1). Codeine is considered a *weak* opioid and is primarily indicated for moderate pain. It has a ceiling effect in that increasing the dose beyond a certain level does not confer greater analgesia, but only an increase in side effects. Propoxyphene is another weak opioid. Standard doses are not much more effective than aspirin or acetaminophen alone, and although still prescribed, prolonged use of it is discouraged, especially in the elderly, for a number of reasons, including the potential accumulation of a metabolite, norpropoxyphene, that can lead to pulmonary edema (abnormal accumulation of fluid in the lungs), cardiotoxicity (toxicity that affects the heart such as heart muscle damage), apnea (slowed or stopped breathing), and death.

The other opioids in Table 1 are prescribed for the treatment of moderate to severe pain. Tramadol is a unique opioid in that it also has serotonergic and noradrenergic actions. Special care must be taken with methadone because of its long, unpredictable

	Average oral dose (in milligrams)	Frequency of dosing (in hours)	Comment
Non-opioids			
Aspirin	325–650	4–6	NSAID; no prescription needed; maximum daily dose not to exceed 4000 mg for analgesia
Acetaminophen (Tylenol)	325–650	4–6	Reduces pain and fever, but not inflammation; no prescription needed; maximum daily dose not to exceed 4000 mg for analgesia
Ibuprofen (Motrin)	200–400	4–6	NSAID; no prescription needed; maximum daily dose not to exceed 1200 mg for analgesia
Naproxen (Naprosyn)	250–500	6–8	NSAID; no prescription needed; initially 500 mg, then 250 mg every 6–8 hours; maximum daily dose (naproxen base) not to exceed 1250 mg for analgesia; also available in controlled-release (CR) form
Diclofenac (Cataflam)	50	6	NSAID; prescription needed; indicated for acute pain, ankylosing spondylitis, primary dysmenorrhea, acute and chronic treatment of osteoarthritis and rheumatoid arthritis; dose listed is for treatment of acute pain and primary dysmenorrhea; maximum daily dose not to exceed 150 mg for acute pain and primary dysmenorrhea; also available in CR form
Meloxicam (Mobic)	7.5	24	NSAID; prescription needed; indicated for osteoarthritis and rheumatoid arthritis; maximum daily dose not to exceed 15 mg
Celecoxib (Celebrex)	200	24	NSAID; prescription needed; selective inhibitor of the COX-2 enzyme; indicated for ankylosing spondylitis, osteoarthritis, rheumatoid arthritis, acute pain, and primary dysmenorrhea; 200 mg/day dose refers to use for treatment of osteoarthritis, different doses used for analgesia or rheumatoid arthritis
Opioids			
Codeine	32–65	4–6	Often used in combination with acetaminophen (Tylenol#3)
Propoxyphene napsylate	100	4	Used alone (Darvon-N) or with acetaminophen (Darvocet)
Oxycodone	5–10	6	Often used in combination with acetaminophen (Percocet), and also available in CR form (OxyContin)
Hydrocodone	5–10	4–6	Often used in combination with acetaminophen (Vicodin, Lortab)
Tramadol	50–100	4–6	Used alone (Ultram) or in combination with acetaminophen (Ultracet), and also available in CR form (Ultram ER)
Meperidine	50–100	5	Not very effective orally, not recommended for chronic use
Morphine	10–30	4–6	Also available in controlled-release formulations
Fentanyl	see comment for dosing	72	Potent synthetic agonist in a CR transdermal system (Duragesic) used for relief of moderately severe to severe pain (dosage range: 12–100 mcg/h), and also available in oral (Actiq) and sublingual form (Fentora) for breakthrough pain
Hydromorphone (Dilaudid)	4–8	4–6	Potent analgesic that tends to be prescribed for severe pain
Methadone (Dolophine)	5–20	8	Very effective analgesic; also used as a substitution pharmacotherapy for opioid addiction
Levorphanol (Levo-Dromoran)	2–4	4–6	Potent analgesic that tends to be prescribed for cancer pain
Oxymorphone CR (Opana)	5–10	12	Doses listed are initial doses for opioid-naïve individuals, also available in IR formulation

Table 1. Food and Drug Administration (FDA)-approved analgesics. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

half-life that could result in drug accumulation and toxicity and because of its potential interaction with other drugs that could either lead to inappropriately low or high blood levels of methadone. Several opioids are available by themselves (i.e., a single entity product) or combined in a formulation that also includes a peripherally acting, non-opioid analgesic (e.g., acetaminophen). The peripheral actions of the non-opioid and the central actions of the opioid complement each other, in that pain is reduced by two separate processes.

Several of the opioids are available in a controlled-release (CR) formulation and are prescribed for the treatment of chronic pain. The product is formulated in such a way that the opioid is slowly released into the bloodstream and can, therefore, provide stable levels of analgesia for a prolonged period of time, ranging from twelve to thirty-six hours. There is another benefit of CR formulations: Patients do not have to awaken during the night to take their medication, unlike many chronic pain patients who are prescribed immediate-release (IR), short-acting opioids. Just as

the non-opioids have risks, so too do opioids. These risks are usually described as *side effects*. Potential side effects include nausea and vomiting, pruritis (itchy skin), mental clouding, constipation, and respiratory depression (decreased breathing). Profound respiratory depression can lead to death.

In hospitals, many patients receive opiates by injection or intravenously. Doses need to be adjusted to compensate for differing distributions and metabolism, but these changes are relatively straightforward for physicians working in the area of pain. Special devices are also available that permit patients to dose themselves, as needed, within specified guidelines. This approach is termed *patient controlled analgesia* (PCA). Even more sophisticated routes of administration are available. Some medications can be injected deep in the back, adjacent to the spinal canal (epidurally) where they can act primarily on the spinal cord. Localizing the medication to the spinal cord can minimize the side effects produced in the brain, such as nausea and respiratory depression.

The chronic use of opioids leads to a lessening of potency, which is termed *tolerance*. To overcome this effect, it may be necessary to increase the dose to maintain a constant level of pain relief (e.g., analgesia). However, many chronic pain patients on long-term opioid therapy can be maintained on a given dose for long periods of time without requiring an increase in the dose. All patients taking sufficient quantities of opioids for an extended time become physically dependent; that is, they experience some withdrawal if the drug is stopped. It is important to distinguish between this physiological process and the process of addiction. A chronic pain patient may be physically dependent on an opioid but not be addicted to the opioid. In the medical community, it is thought that most patients on chronic opioid therapy with no prior history of substance abuse are not addicted; that is, they do not exhibit impaired control over their opioid use, do not use compulsively, and do not crave opioids. However, it is also acknowledged that misuse and abuse does occur in some chronic pain patients. One known risk factor for abuse of opioids in chronic pain patients is a history of substance abuse. That does not preclude such patients from long-term opioid therapy but does necessitate closer and more frequent monitoring of the patient on the part of the medical caregiver. Such monitoring could involve urine toxicology screening and behavioral contracting.

In the late 1990s, drug abuse epidemiological networks detected increasing prevalence of nonmedical use of prescription opioids. This pattern was ascertained independently by drug abuse surveys, the number of emergency room visits associated with nonmedical use, and the number of admissions to drug abuse treatment facilities. As of 2006 (the most recent year as of 2008 for which epidemiological data are available), the prevalence of nonmedical use of prescription opioids remained substantially elevated and was of great concern to those in the medical, public health, drug abuse prevention, and law enforcement fields.

The nonmedical use is seen in all age groups, including children and adolescents. In 2006, 5 percent and 10 percent of U.S. high school seniors reported taking OxyContin (controlled-release formulation of oxycodone) and Vicodin (hydrocodone/acetaminophen), respectively, that was not prescribed to them. The increase in nonmedical use was thought to be related to increased medical use of the prescription opioids. For many years pain was grossly undertreated in the United States, but through educational efforts and public health initiatives, including mandating that patients be asked about their pain in hospitals, pain is being treated more aggressively, with increased prescribing of opioids when such drugs are indicated. The increased use of opioids for licit purposes, though, increases the amount of opioids available for diversion to nonmedical use.

The means by which prescription opioids are diverted are many and include a family member or friend giving them to other people, a person stealing another person's medication from the medicine cabinet, doctor shopping (a practice, or more aptly put a *scam,* in which a person not necessarily in pain gets opioid prescriptions from multiple doctors by complaining of a painful condition in which opioids might be indicated), and pharmacy and warehouse thefts. There is no simple solution to the problem of nonmedical use of prescription opioids. Reducing the amounts of opioids that are available for medical use might decrease the prevalence of nonmedical use but would deprive patients who need these medications for adequate pain relief. As of 2008, some pharmaceutical companies were working to develop

opioids that may have less abuse liability by altering their formulation, but such attempts remained in preliminary phases. It was anticipated that nonmedical use of prescription opioids would continue to be a serious problem in the United States for some years to come.

See also **Abuse Liability of Drugs: Testing in Humans; Addiction: Concepts and Definitions; Controlled Substances Act of 1970; Pain: Behavioral Methods for Measuring Analgesic Effects of Drugs; Tolerance and Physical Dependence.**

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PAKISTAN. *See* **India and Pakistan.**

PAPAVER SOMNIFERUM. Poppy plants, of the genus *Papaver*, are long-stalked flowers of varying colors encompassing approximately 140 species. Of the many types of poppy plants, *Papaver somniferum* is known as the opium poppy. It has white or blue-purple flowers and is widely cultivated in Asia, India, and Turkey, which supply much of the world's opium. Cultivation requires a tropical or subtropical climate without excessive rainfall. In the Northern Hemisphere, the plant flowers in late spring, after which the petals fall in a short time. Flowering is followed by the rapid growth of the

capsules (the plant's ovaries) for about two weeks. Incisions are carefully made in the capsule to obtain the milky juice, which is then dried as a gum that yields opium. The yield of opium can vary widely, but is typically about five pounds (2.25 kilograms) per acre.

The opium serves as a source of morphine, codeine, and thebaine and is widely used in the production of important painkillers (analgesics).

Typically, morphine comprises 10 percent of opium. Most of the morphine used in medicine is obtained by purifying opium.

Illicit uses of opium are also widespread. In many parts of the world, opium is still smoked or eaten. Morphine extracted from opium may in turn be converted to heroin in clandestine laboratories. Heroin is the major opioid used illicitly in the United States. To prevent the collection and sale of opium for illicit conversion to heroin, new ways of processing the poppy plant have been developed. The most widely used consists of mowing the poppy fields before the pods are ripe enough to yield opium. The mowed stems, immature pods, and plant matter, referred to collectively as poppy "straw," are then shipped in bulk to large processing centers where the active alkaloids are extracted under careful supervision.

Other species of *Papaver* also contain alkaloids that can be converted into potent opioids. For example, *Papaver bracteatum* contains high concentrations of thebaine, which can be used to produce compounds several hundred times more potent than morphine.

See also **Crop Control Policies; Golden Triangle as Drug Source; International Drug Supply Systems; Opiates/Opioids; Pain, Drugs Used for.**

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GAVRIL W. PASTERNAK

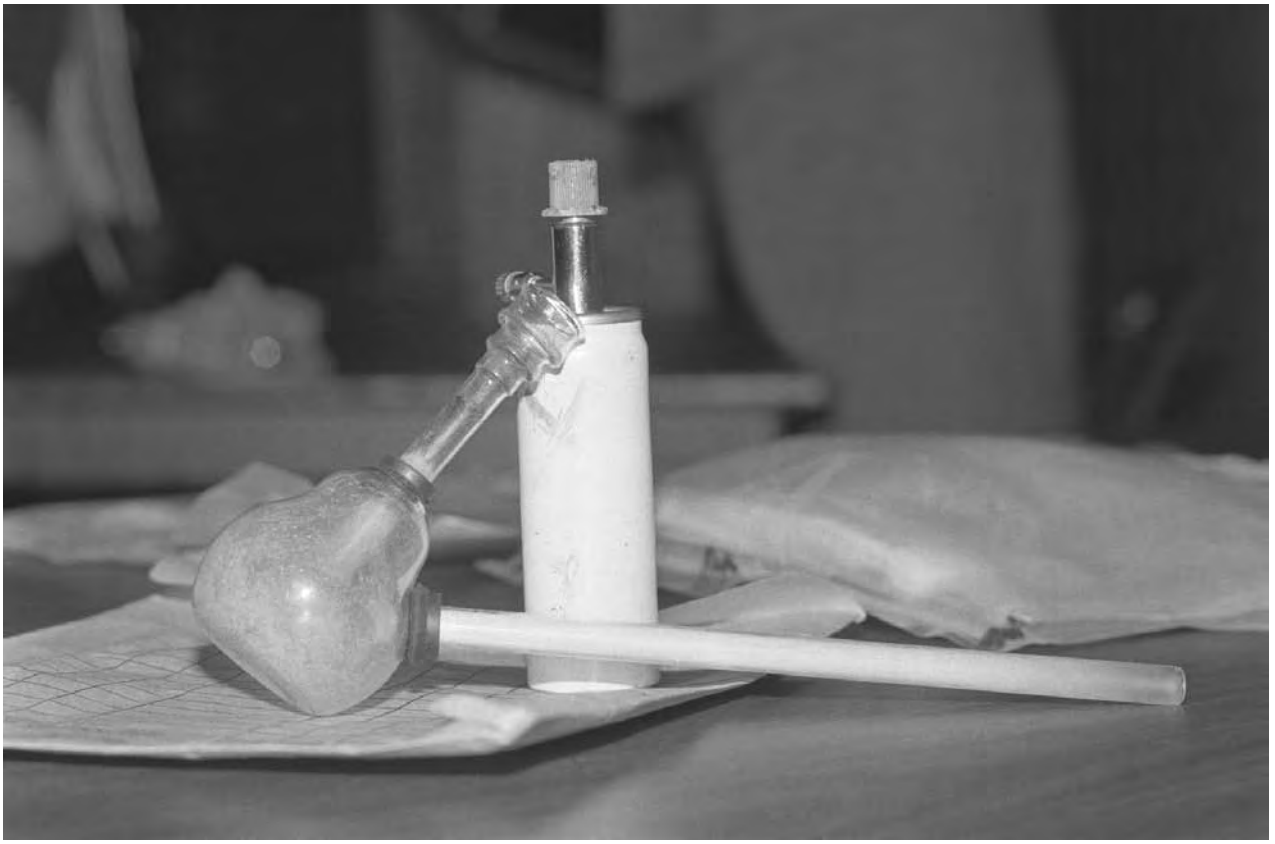
PARAPHERNALIA, LAWS AGAINST.

Drug paraphernalia includes equipment, products, and materials that facilitate or enable the making, using, or concealing of illicit drugs. Some paraphernalia, such as hypodermic syringes for heroin and pipes for smoking marijuana, are used by consumers of drugs. Equipment such as scales, vials, and baggies, as well as chemicals used to dilute drugs, are examples of paraphernalia used by dealers of illicit drugs. The Federal Drug Paraphernalia Act, which is part of the Controlled Substances Act, makes it illegal to possess, sell, transport, import, or export drug paraphernalia as defined by the statute. In addition, laws prohibiting the possession and use of paraphernalia have been adopted in every state. Though constitutional objections have been raised against these laws, the U.S. Supreme Court has declined to strike down such statutes.

The first drug-paraphernalia laws, prohibitions against possessing opium pipes, were enacted by western states in the late nineteenth century as part of broad statutory efforts to suppress opium smoking by Chinese immigrants. During the first third of the twentieth century, some states, in conjunction with a legislative attempt to criminalize the nonmedical use of opiates and cocaine, also prohibited the possession of hypodermic syringes without a medical prescription. By 1972, when the National Commission on Marijuana and Drug Abuse conducted a survey of state drug laws, about twenty states had adopted some type of drug-paraphernalia prohibition.

Commercialization of drug paraphernalia, especially through so-called head shops, in the early 1970s triggered a new generation of paraphernalia prohibitions, many of which criminalized the sale as well as possession of these articles. Such laws attempted to enforce comprehensive bans on drug-related devices or articles intended for use with illicit drugs.

The drug-paraphernalia industry responded to the enactment of these laws by challenging their constitutionality on grounds of vagueness and overbreadth. In most cases, courts struck down the laws as unconstitutionally vague. First, they applied to objects that had lawful as well as unlawful



Crack cocaine pipe. © BETTMANN/CORBIS.

uses, so these laws failed to provide fair notice of prohibited conduct. Second, the lack of explicit standards left police with discretion to enforce these laws in an arbitrary and discriminatory manner.

Since the late nineteenth century, the federal and state governments have enacted laws to regulate the possession and sale of drug paraphernalia, like the crack pipe pictured in Figure 1.

In 1979 the U.S. Drug Enforcement Administration (DEA) responded to these legal defeats by drafting a model law that could withstand constitutional scrutiny and at the same time effectively combat the drug-paraphernalia trade. The DEA drafted the Model Drug Paraphernalia Act (MDPA), which explicitly requires prosecutors to prove that the defendant knew the alleged paraphernalia would be used with illegal drugs. The addition of this intent requirement was designed to alleviate the fair-warning concern associated with the earlier generation of statutes. In addition, the MDPA attempts to provide a more specific definition of drug paraphernalia by listing objects included within the category and by providing factors that judges should consider in determining whether an object falls within the definition. Finally, the act prohibits placement of an advertisement when one knows, or "reasonably should know," that it is intended to promote the sale of objects "designed or intended for use as drug paraphernalia."

During the 1980s, most states enacted the MDPA or an equivalent statute, and legal challenges soon followed. In 1982 the Supreme Court upheld a local ordinance that required businesses to obtain a license in order to sell articles designed to be used with illegal drugs. Although this law did not involve a criminal statute prohibiting sale or possession of paraphernalia, lower courts subsequently upheld criminal laws modeled after the MDPA against vagueness and overbreadth challenges. In 1994 the Court addressed many of the MDPA issues when it reviewed the constitutionality of the Mail Order Drug Paraphernalia Control Act, which was part of the Anti-Drug Abuse Act of 1986.

This federal statute, which is modeled on the MDPA provisions, makes it a crime to use the U.S. mail to facilitate the sale and distribution of drug paraphernalia. The Court held that the statute was not unconstitutionally vague and that the seller need only be aware that customers in general are likely to use the merchandise with drugs. This reading of the intent requirement was a victory for law enforcement.

In the wake of the HIV/AIDS epidemic, another feature of traditional drug-paraphernalia laws has become controversial. In an effort to reduce the risk of transmission of the human immunodeficiency virus (HIV) and other blood-borne diseases among needle-sharing illicit drug users, state and local public-health authorities have sought to establish clean-needle exchange programs, usually through hospitals and clinics. To implement these programs, lawmakers have had to repeal the paraphernalia laws or prosecutors have agreed not to enforce them in this context. Many states and local governments have refused to support needle-exchange programs, and the federal government has not funded them due to concerns that dispensing needles will encourage illicit drug use. However, the National Academy of Sciences has concluded that these programs reduce the risk of HIV transmission and has found no evidence that they encourage drug use.

In general, drug-paraphernalia laws represent a type of drug legislation aimed mainly at declaring and symbolizing society's intolerance of illicit drug use. However, in 2003 the federal government's Operation Pipedream led to numerous criminal charges against eighteen companies selling drug paraphernalia. These companies accounted for annual sales of $250 million. With the decriminalization or reduction in severity of criminal sanctions for possession of small amounts of marijuana, local law enforcement agencies have used paraphernalia laws as a way of exacting heavier criminal penalties. These laws are subject to highly discretionary enforcement and can have unintended costs or ramifications.

See also **Legal Regulation of Drugs and Alcohol; Needle and Syringe Exchanges and HIV/AIDS; Parent Movement, The; Substance Abuse and AIDS.**

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PAREGORIC. Paregoric is a camphorated opium tincture. Tinctures of opium are alcoholic extracts of opium, widely used in the treatment of diarrhea. Paregoric contains powdered opium, anise oil, benzoic acid, camphor, glycerin, and diluted alcohol. With only 0.4 milligrams per milliliter of morphine in 45 percent alcohol, it is more dilute than opium tincture—and the taste of the camphorated formula is generally disliked, helping to minimize excessive use or abuse.

Although paregoric is not indicated for bacterial or parasitic causes of diarrhea, it can be very helpful for other causes. Taken orally, it effectively slows down the gastrointestinal transit of wastes and enhances resorption of fluid from the intestine. Doses that effectively treat diarrhea typically do not cause euphoria or analgesia; however, excessive doses can be abused and can lead to dependence.

See also **Dover's Powder; Laudanum; Opiates/Opioids.**

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GAVRIL W. PASTERNAK

PARENT MOVEMENT, THE. Several national organizations trace their origins to the Parent Movement of the 1970s and 1980s. As of 2008, the most prominent was National Families in Action whose founder, Sue Rusche, remained active in efforts to prevent drug use and abuse among young teenagers and pre-teens. The grassroots movement began with a group of concerned parents in then-president Jimmy Carter's home state of Georgia in 1976. At the time, these people believed children's drug use, particularly marijuana smoking, had reached unprecedented levels and officials and agencies of the Carter administration were communicating an attitude of complacence with respect to so-called recreational drug use that the parents found offensive and frightening.

Marsha Keith Schuchard and her husband, Emory University professor Ronald Schuchard, discovered that their eldest daughter and most of her friends were using drugs at the daughter's 13th birthday party. In response, the family organized the nation's first parent-peer group. Such groups consisted of parents whose children were each other's friends. They came together to establish age-appropriate social and behavioral guidelines for their children to help them avoid unhealthy and destructive behavior. Marsha Keith Schuchard, using the name Marsha Manatt, later wrote about this experience in *Parents, Peers and Pot*, a book the National Institute on Drug Abuse published and distributed free to the more than one million people who requested it during the 1980s.

At first, the parents confronted public attitudes that were not in their favor. In August 1977, President Carter endorsed decriminalization of marijuana, and opinion polls registered widespread acceptance of the idea. Nevertheless in the fall of 1977, the group of Atlanta citizens, who had begun meeting the previous year, formed National Families in Action. Founders included Marsha Keith Schuchard and Sue Rusche, who later became the organization's executive director. This organization called attention to the social and environmental factors that seemed to promote the use of illicit drugs. Its purpose was twofold: 1) to replace commercial and societal messages that glamorize drug use with accurate information based on scientific research about drug effects, and 2) to help people put this information to use by organizing community-based parent drug-prevention groups.

One target of the founders of National Families in Action was the drug paraphernalia shops, called head shops (drug users called themselves *heads, acid heads, pot heads, coke heads*). These shops offered drug-themed magazines, books, and colorful and attractive gadgets that appeared to the concerned parents to appeal particularly to impressionable youth.

In January 1978, the Georgia State Legislature passed the nation's first laws banning the sale of drug paraphernalia, thanks in large part to the lobbying activities of National Families in Action. At about the same time, Otto and Connie Moulton, of Danvers, Massachusetts, founded Committees of Correspondence. Their goal was to alert citizens about the activities of drug-culture and drug-policy organizations that advocate the decriminalization and legalization of illicit substances. They began sending out packets they called Otto Bombs, detailing information about the local, state, and federal lobbying activities of drug-legalization organizations such as National Organization for the Reform of Marijuana Laws (NORML), whose board and advisory committee at the time consisted of many drug-paraphernalia manufacturers and publishers. Patterned after the original Committees of Correspondence founded before the Revolutionary War, the modern version sought to uphold the rights of citizens to be drug free. A periodic newsletter presented information from researchers and doctors refuting medical and scientific claims made by legalization proponents. Committees of Correspondence also tracked the lobbying efforts of other organizations (such as NORML) that advocated legalizing drugs.

In the spring of 1978, NORML began to make issue of a U.S. supported crop eradication program in Mexico that involved spraying drug crops with the poison, Paraquat. NORML threatened to sue the government on the basis that the program endangered the health of American marijuana smokers. That people who were willfully breaking the law deserved protection and that officials of the federal government were making overly sophisticated distinctions among which drugs were dangerous and which were not was just too much for many people and the tide of opinion began to change.

In April 1978, Thomas Gleaton invited Keith Schuchard and Sue Rusche to address the Fourth

Annual Southeast Regional Drug Conference. Gleaton held the conference for drug education professionals at Georgia State University, where he taught. He also invited officials from various federal agencies. Many accepted, particularly from the National Institute on Drug Abuse. The Parents' Resource Institute for Drug Education (PRIDE) was founded in the summer of 1978, following this conference. Publicity generated by the passage of Georgia's drug paraphernalia laws, by the Fourth Southeast Drug Conference, and, later, by the publication of *Parents, Peers and Pot,* brought requests for help from parents throughout the United States. These parents wanted to form groups to ban drug paraphernalia sales in their cities and states and to prevent substance abuse among local children. For the next several years, leaders from National Families in Action, PRIDE, Committees of Correspondence, and other national organizations, along with leaders of emerging groups from various states, traveled across the nation helping parents form prevention groups. Funding from the National Institute on Drug Abuse made it possible for parent group leaders to travel to communities that sought their help. One of the first groups to form outside Georgia was Naples (Florida) Informed Parents, led by Pat and Bill Barton. The Florida leaders joined those from Georgia and Massachusetts to help parents in other states form similar groups.

In the summer of 1978, Carter's health advisor and so-called drug czar, Peter Bourne, was forced to resign amid allegations that he had written a fraudulent prescription for a staff member and even that he, himself, had used cocaine. This event marked the end of an era although the shift would not be immediately apparent. Lee Dogoloff, Bourne's deputy and successor, was instrumental in raising the profile of the Parent Movement among federal officials and in supporting the movement's efforts to influence federal publications on drugs and drug-use prevention. He also helped carry the movement's message to members of Congress through testimony at a number of hearings.

In January 1979, Senator Charles Mathias (D-MD) held congressional hearings on the harmful effects of marijuana and invited many parent-group leaders, along with scientists, to Washington to testify. The parent leaders took advantage of this opportunity to be together for the first time; they discussed the need to form a Washington-based organization that could represent their interests with both Congress and the federal agencies that were making and implementing national drug policy. They agreed to meet at the Fifth Annual Southeast Regional Drug Conference, later known as the PRIDE conference, in Atlanta in the spring of 1979. There, they founded the National Federation of Parents for Drug-Free Youth. Pat and Bill Barton were elected as the group's co-presidents and a Maryland parent group leader, Joyce Nalepka, later became the Federation's executive director.

During the presidential election campaigns that began in the summer of 1979, parent groups worked hard to get drug-abuse prevention policy on the agendas of presidential candidates. After the inauguration of Ronald Reagan (January 1981), the parent movement found that it had natural allies in the White House: Both President Reagan and First Lady Nancy Reagan were sympathetic to its cause. The National Federation of Parents for Drug-Free Youth led a massive letter writing campaign to the president-elect asking him to bring Carlton Turner to the White House as his drug-policy advisor. Turner, of the University of Mississippi, was responsible for growing marijuana used in scientific research. He had devoted much time to educating parents at various conferences about the pharmacological effects of marijuana on the brain and body and had earned their trust. President Reagan acted on the Federation's appeals and selected Turner as his drug advisor. Shortly after the inauguration, Turner helped the federation arrange for parent-group leaders to brief Mrs. Reagan on the prevention movement and enlist her support for their cause. She responded positively and served informally as the national spokesperson for the parent drug prevention movement.

A few years later, President Reagan appointed parent-group leader Ian Macdonald, a pediatrician from Florida, to serve as administrator of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), the federal agency in the Department of Health and Human Services that was responsible for substance abuse and mental health research and services. One of Macdonald's legacies is the Center for Substance Abuse Prevention (then called the Office for Substance Abuse

Prevention, or OSAP), which he created as an office during his tenure at ADAMHA. Congress formally authorized OSAP as a center, changed its name to CSAP, and funded it in the Anti-Drug Abuse Act of 1986. Through this kind of concerted effort, parents were able to influence the appointments of key policymakers in the federal government to emphasize and implement their goals: to mitigate the use of illegal drugs (and alcohol and tobacco among underage individuals), to help drug users quit, and to find treatment for those who are addicted and cannot quit by themselves. Beginning in the late 1980s, the Center for Substance Abuse Prevention made demonstration grants available to support local, grass-roots, drug prevention efforts targeting high-risk youth, primarily in African American, Hispanic, Asian American, and Native American communities.

The Parent Movement struggled in the following decades. According to the Monitoring the Future survey funded by the National Institute on Drug Abuse, annual use of marijuana, cocaine, and heroin reached a low point in the early 1990s but rose among children at all grade levels at least until 1997 when it seemed to level off. Despite determined attempts at the end of that decade by the CSAP director at the time, Karol Kumpfer, to enlist support from parents, the response was mainly from people who had been involved in the original movement and were now grandparents. It seemed that the grass-roots style and zero-tolerance approach characteristic of the Parent Movement lacked appeal to a new generation of parents.

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SUE RUSCHE
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PATHOLOGICAL GAMBLING (PG). *See* **Gambling.**

PEMOLINE. Pemoline is a stimulant medication. Although not structurally similar to the amphetamines, pemoline has similar psychomotor stimulant effects but only minimal effects on the cardiovascular system. Pemoline is often used therapeutically (despite being less effective than amphetamine or methylphenidate) in the treatment of attention deficit/hyperactivity disorder (ADHD)—a syndrome that first becomes evident during childhood and is characterized by excessive activity and difficulty in maintaining attention. Pemoline has the advantage of a long half-life, which means that dosing can be once daily, but clinical improvement can be delayed by three to four weeks after initiation of pemoline therapy. In addiction, the likelihood for abuse of pemoline appears to be substantially less than that of the amphetamines.

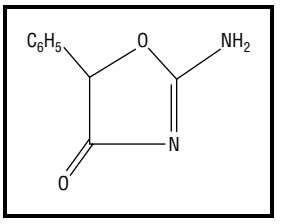

Figure 1. Chemical structure of pemoline. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Attention Deficit Hyperactivity Disorder; Psychomotor Stimulant; Schizophrenia.**

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MARIAN W. FISCHMAN

PERCEPTION AND EFFECTS OF DRUGS.

See **Sensation and Perception and Effects of Drugs.**

PERSONALITY DISORDERS.

Personality disorder (PD) refers to a pattern of behavior and perception that deviates from the expected cultural norms and is "inflexible and pervasive across a broad range of personal and social situations" (*DSM-IV-TR*, p. 689). As with all DSM disorders, a diagnosis of a specific personality disorder requires that the symptoms cause significant distress or functional impairment. The diagnosis is made only in individuals who are at least 18 years old. In *DSM-IV*, diagnostic categories are intermittent syndromes characterized by a set of symptoms. *DSM-IV personality disorder* describes a set of traits that tend to be more stable over time than symptoms associated with other *DSM-IV* disorders. The *DSM-IV* describes ten independent categories of personality disorders, each containing a unique set of symptoms. The *DSM-IV* also provides a dimensional model in which the ten personality disorders are grouped into three clusters based on their similarities: odd-eccentric, dramatic-emotional, and anxious-fearful. The dimensional model of personality disorders posits that maladaptive personality traits are expressed on a continuum from normal personality to personality disorder. According to the dimensional model of personality disorders, many traits are shared among the personality disorder diagnostic categories. Table 1 provides PDs in each cluster and their shared characteristics.

PREVALENCE AND COMORBIDITY

The prevalence and comorbidity of PDs has been studied in patient groups and in the general population. In the 2001–2002 NIAAA *National Epidemiologic Survey on Alcohol and Related Conditions* (NESARC; Grant et al., 2004), 14.7 percent or 30.8 million adults reported at least one of the seven PDs assessed (paranoid, schizoid, antisocial, histrionic, avoidant, dependent, obsessive-compulsive). Obsessive-compulsive personality disorder was the most prevalent (7.9%) followed by paranoid (4.4%), antisocial (3.6%), schizoid (3.1%), avoidant (2.4%), histrionic (1.8%), and dependent (0.5%). Gender differences were evident, with women at significantly greater risk for avoidant, dependent, and paranoid PD, and men at significantly greater risk for antisocial PD. Blacks, Native Americans, Asians, and Hispanics were at significantly greater risk for schizoid PD than whites. Native Americans were at significantly greater risk for antisocial PD than whites (Grant et al., 2004). People with higher education (bachelor's degree or higher) were at lower risk for all PDs compared to those with lower levels of education. All seven PDs were highly associated with other PDs in each *DSM-IV* cluster as well as with other PDs (Grant et al., 2005). The high comorbidity across personality disorders suggests that each PD is a different manifestation of a shared underlying disorder, an approach that supports the dimensional model described above.

A NESARC study of personality disorders and Axis I comorbidity supported earlier findings from treatment studies of high rates of personality disorders among individuals with mood and anxiety disorders (Grant et al., 2005). Among NESARC respondents with a current mood or anxiety disorder, the prevalence of at least one PD was 46.8 percent and 41.8 percent, respectively. Among individuals with a mood or anxiety disorder, obsessive-compulsive, paranoid, and avoidant PDs were the most prevalent. Avoidant (ORs = 10.6–14.5) and dependent (ORs = 12.2–22.0) PDs were most strongly related to major depression, dysthymia, and mania. With respect to anxiety disorders, avoidant and dependent PDs were more strongly related to each of the anxiety disorders than any other PD (Grant et al., 2005). Nearly 53 percent of NESARC respondents who sought treatment for a mood disorder in the last 12 months had a personality disorder. Among those who sought treatment for an

Cluster	Personality disorder	Characteristics
A - odd-eccentric	Paranoid, Schizoid, Schizotypal	Suspicious, mistrustful, hypervigilant, easily offended, unfeeling toward others, withdrawn and isolated, odd and eccentric behavior
B - dramatic-emotional	Antisocial	A pervasive pattern of behavior that includes: lying, theft, violence, substance abuse, sexual promiscuity, spouse and/or child abuse, inconsistent work, legal conflicts, impulsivity and lack of remorse for antisocial acts
	Borderline	Unstable mood, behavior, relationships, and self-image; impulsive, self-destructive (e.g., suicide attempts, 'cutting,' substance abuse), chronic feelings of emptiness, low tolerance for being alone
	Histrionic, Narcissistic	Dramatic, emotional, erratic, seductive, attention-seeking, exaggerated sense of self-importance, feelings of entitlement, exploitation of others, lack of empathy, difficulty accepting criticism, disregard for social conventions.
C - anxious-fearful	Avoidant, Dependent, Obsessive-compulsive	Timid, extreme sensitivity to real or imagined rejection, socially withdrawn, low self-esteem; avoidance of assuming responsibility for life events and goals, dependence on others to make everyday decisions; passive, submissive, discomfort when alone; perfectionist, orderly, inflexible, indecisive, constricted emotions, obstinate, overly conscientious

Table 1. *DSM-IV* dimensional model for personality disorders. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

anxiety disorder, nearly 60 percent had a personality disorder (Grant et al., 2005). These high comorbidity rates are a concern to treatment providers because of conflicting evidence regarding the effects of co-occurring PDs on outcomes of treatment for mood and anxiety disorders. In earlier studies, PDs were found to complicate treatment outcomes (Alnaes & Torgersen, 1997; Baer et al., 1992; Turner, 1987) while subsequent studies showed that pharmacotherapy for major depression appears to improve PD symptomatology as well (Fava et al., 2002; Hirschfeld, 1999).

In the *Collaborative Longitudinal Personality Disorders Study* (CLPS; Gunderson et al., 2000) schizotypal, avoidant, borderline, and obsessive-compulsive PDs were assessed in treatment-seeking patients. In this study, the mean number of co-occurring personality disorders was 1.4, with 26 percent reporting borderline PD, 24 percent reporting avoidant PD, 23 percent reporting obsessive-compulsive PD, and 13 percent reporting schizotypal PD (Skodol et al., 2005). Borderline PD was significantly associated with substance use disorders and PTSD; and avoidant, borderline, and dependent PDs were associated with depression. When compared to Caucasian patients, African American patients had proportionally higher rates of schizotypal PD and Hispanic patients had higher rates of borderline PD. Among individuals with borderline PD, there was a higher rate of substance abuse in men, and higher rates of Post Traumatic Stress Disorder (PTSD) and eating disorders in women.

TREATMENT

Strong empirical evidence supports psychotherapy, primarily psychodynamic and cognitive-behavioral approaches, as the treatment of choice for personality disorders when reduction in symptoms as well as improvement in social and occupational function are the targeted outcomes (Verheul & Herbrink, 2007). For psychotherapy conducted on an outpatient, individual basis, there is no evidence to support a difference in the efficacy between psychodynamic and cognitive-behavioral theoretical frameworks. Evidence for the efficacy of psychodynamic, long-term outpatient group psychotherapy is suggested in a number of studies but not as a stand-alone treatment for individuals with severe personality pathology who may have low tolerance for anxiety and frustration. For these patients, embedding group treatment into day-hospital treatment or adding

individual sessions is recommended (Verheul & Herbrink, 2007). In terms of specific clusters of personality disorders, research suggests that short-term, psychodynamic psychotherapy in a day-hospital setting is more effective for Cluster C personality disorders than the disorders in the other clusters. It is suggested that day-hospital treatment be followed up with long-term individual or group psychotherapy to yield continued improvements in occupational and social functioning. Evidence suggests that inpatient psychotherapy is effective for all PDs and that a shorter inpatient phase (3–6 months vs. 12 months) followed by a long-term outpatient phase (e.g., 12 months) is preferable to a long-term inpatient phase with no outpatient follow-up. (For a thorough review of efficacy of modalities of psychotherapy for personality disorders, see Verheul & Herbrink, 2007.) Some research has begun to investigate the added value of psychopharmacological treatment with psychotherapy, but there is as of 2008 only limited evidence to support the use of medication as a treatment for personality disorder symptoms.

See also **Attention Deficit Hyperactivity Disorder; Conduct Disorder and Drug Use; Epidemiology of Drug Abuse; Risk Factors for Substance Use, Abuse, and Dependence: Personality.**

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SHARON SAMET

PERU. Peru is a South American republic of about 500,000 square miles, bounded by the Pacific Ocean on the west, Ecuador and Colombia on the north, Bolivia and Brazil on the east, and Chile on the south. The country's varied elevation makes for three drastically different climatic zones. Along the west is a narrow and extremely dry desert; down the middle run two chains of the rugged Andes Mountains, with a high cold plateau between them; and to the east sprawls the hot, flat, forested headwaters of the Amazon. A variety of drugs have played important roles in the lives of the Peruvian people since ancient times. The little

epidemiological data that exist are fragmentary and unreliable, while ethnographic studies are often richly detailed but only local in scope. However, much of the behavior associated with drugs in Peru in modern times is public and has been discussed by local writers.

COCA AND COCAINE

Coca is undoubtedly the most commonly used drug in Peru, and it plays a major role in the nation's culture. Cocaine, by contrast, is rarely used by Peruvians, but it is very significant in the illegal economy. Thus, the problems associated with coca do not derive from its traditional use but from the global market for its derivative, cocaine hydrochloride. Cocaine use and the big money and varied crimes associated with it have overshadowed the ancient origins and respectable cultural roots of coca (*Erythroxylon coca*). The coca bush grows best in a small subtropical portion of the eastern slopes of the Andes, and its leaves have been used and widely traded over a broad area for at least 1,000 years. Its early uses probably differed little from today's customary uses.

The leaves of the coca plant are routinely "chewed" (or, more accurately, sucked), and it is considered a refreshing dietary supplement. Its use is medicinal and healthful, as well as symbolic and mystical. Far removed from the derivative drug cocaine, coca produces neither the "rush" nor the "high" commonly associated with illicit drugs.

A cud, or quid, anywhere from the size of a peach pit to the size of a golf ball, can be gradually built up by tucking the plant's leaves into one's cheek. Throughout the day, the cud can occasionally be freshened by the addition of a few new leaves, or by the ingestion of a pinch of lime (i.e., ground shell or stone). Although it is mostly used by adult males, coca is by no means off-limits to others. Chewing coca leaves is most common among small-scale agriculturalists, but the habit has been brought to urban areas by migrants, where it is slowly being adopted as an occasional recreational activity.

Although the behavior of users shows little effect, scientific analysis supports subjective accounts that chewing coca helps to relieve hunger and thirst, as well as cold and fatigue. Calcium (from the lime), glucose, and a few vitamins that are lacking in the diet of the poor are beneficial, and there is no indication of any harms.

Coca leaves also have religious and magical uses among the native population. Coca is an ideal sacrifice or offering to the spirits and deities that are thought to inhabit the area and affect the lives of people. It is also used for divining by specialists who are said to know how to "read" scattered leaves. Such mystical associations strengthen support for coca, even among those who do not routinely chew it.

Tourists in Peru may occasionally be surprised to see coca tea offered in fancy hotels and restaurants, but this brew is said to be a cure or palliative for *sorroche*, the altitude sickness that newcomers often suffer when adjusting to a deficit of oxygen at high elevations. This condition is marked by heart palpitations and headache. Since about 2000, small amounts of coca have also been incorporated in some toothpastes, cookies, and other products, but these account for only a small portion of total production.

In addition to the legal market, coca growing has expanded for clandestine purposes, particularly since about 1980. The leaves are carried to the eastern lowlands, where, under the cover of the jungle, scattered encampments are devoted to production of cocaine paste. Soaking about a ton of coca leaves in kerosene or diesel fuel and sulphuric acid yields about twelve pounds of this paste, which in its crudest form is called *bazuco*. It is often mixed with tobacco in cigarettes (also called *bazuco*), and smoked by poor young people in urban slums throughout the country. This use is harmful to the individual smoker, but it is of negligible importance on the national scene. A more refined paste is generally flown clandestinely to Brazil or Colombia, where it is further processed to yield about one-third as much of the familiar white street drug, which is sold internationally to wealthy recreational users or desperate addicts.

ALCOHOLIC BEVERAGES

Not all Peruvian beverages that contain alcohol are habitually drunk with the aim or result of intoxication. For a significant portion of the population (notably Quechua and Aymara speakers), home-brewed beer is a dietary staple drunk by people of both sexes and all ages, often with meals or as a

refreshing beverage at other times. Generically known as *chicha*, it is most often made from maize, although other grains, as well as various fruits and vegetables, may also be fermented. Regional and seasonal special *chichas* are greatly appreciated. With an alcohol content rarely above 4 percent, casual drinking is healthful because *chicha* is rich in some vitamins and nutrients that are scarce in the restricted diet of the nation's working class.

Most *chicha* is brewed at home in small batches for use as a basic food or for the celebration of special events. Some urban breweries produce larger batches, with more quality controls, but this is still for local consumption only, because the product spoils too rapidly to be transported for broader distribution. It also figures prominently in the Andean tradition of labor exchange. Often, a short period of pooled effort is required for work such as thatching a roof, sowing or harvesting a field, or threshing grain. People take turns working on each other's properties, with each individual alternating as host and guest for the chicha drinking that accompanies or follows such work.

In the wake of the Spanish Conquest, Catholic missionaries brought grapevines to the Americas in the hope of producing wine for ceremonial use by the native peoples, whom they hoped to convert. Grapes took root in Peru in the 1550s, but only in the twenty-first century have a few Peruvian vineyards begun to produce palatable wines, and these still have only a small internal market and are rarely exported.

Since refrigeration became affordable in commercial outlets, lager beer, which is produced by a few breweries throughout the country, has been an occasional refreshment, especially on hot days. However, this beverage plays little part in the lives of most Peruvians, as is also the case with a variety of distilled beverages. Such spirits were unknown in the area in pre-Columbian times, but they were introduced early in the colonial period (1500s). *Trago*, a crude rum distilled from sugarcane juice, is commonly used as a shortcut to drunkenness, and it is actively, though episodically, sought and appreciated by both males and females in many Indian communities, especially on religious holidays. Few claim to enjoy *trago*, but drinkers of the rum often boast of an almost mystical transcendence, and they habitually spill a little on the ground or floor to share with Pachamama (the great Earth-Mother) before each drink. A form of whiskey is often passed off as various internationally famous brands and predominates in occasional celebratory drinking by wealthy urbanites. The local grape brandy, *pisco*, has gained some popularity among a few connoisseurs.

TOBACCO AND SNUFFS

Although this is one of the regions from which the plant containing nicotine (*Nicotiana spp.*) appears to have originated 3,000 years ago, local populations smoke little tobacco in cigarettes, cigars, or pipes. In the eastern lowlands there are many small groups of relatively isolated peoples (often called "indigenous" or "tribal" peoples), and it is customary for adult males to occasionally take snuffs in large doses. Often psychoactive, these snuffs have a number of ingredients derived from various plants of the tropical forest. There are minor variations in the means of administration, and in the effects they produce, but they are all used only on special occasions, and none of them result in addiction or in social, psychological, or other problems. Snuffs are sometimes used for artistic inspiration, predicting the future, or communicating with spirits that are thought to provide moral and religious guidance. Some of the alkaloids they contain are said to induce the sense of flying, while others produce visions of jaguars, but most result in immensely varied sensations that users interpret in diverse ways. A common theme is that of transcending ordinary reality.

In some populations in Peru, boys have a dramatic single exposure to such drugs at their initiation into adulthood, during which they first encounter the jungle animal that will be their ally or counterpart throughout life. More often, however, the use of these drugs is reserved for shamans, who are thought to have divinatory and supernatural powers. Because they supposedly can fly as well as communicate with animals, ancestors, and other spirits, shamans often serve as curers or fortune-tellers in public or private ceremonies.

One of the most popular snuffs is *ayahuasca*, or *yaje*, which is often called "the vine of souls." Its source is the jungle vine *Baniosteriopsis caapi*, and it contains both harmine and ibogaine alkaloids. Archeological remains show it was used 5,000 years ago, and it

remains important today. Elaborate formal rituals accompany its ingestion, and a cult of "drug tourism" has grown up around it in the city of Iquitos. Shamans with specialized knowledge use it for the diagnosis and curing of disease, whereas dabblers claim that it bestows an incredible sense of transcendence.

Another of the more widespread snuffs is *ebene*, which is derived from the bark and resin of the tree *Virola theidora*. Mescaline, famous elsewhere as a derivative of peyote, is derived from the root of the San Pedro cactus (*Tricocereus pachanoi*), although cannabis, or marijuana, is strangely rare in Peru. *Huilca* (or *vilca*), which is derived from seed pods of the tree *Anadenanthera colubrina*, was at one time ingested via enema by the Inca, and it is still popular among many Amazonian groups. The deadly nightshade (*Atropa belladonna*) contains the mind-altering alkaloid scopolamine. One must be extremely careful when ingesting these last two substances, for only a minute difference in dosage could result in an agonizing death.

With few exceptions, the complex botany and chemistry of such preparations is still not fully understood, and scientists wonder at how so many and such complex concoctions could have been invented. Some contain several ingredients, each prepared in a special way and processed for a specific time. Others contain a single element that gives the blend its specific effect within the human body, while some others would be inactive (or deadly poisonous) if they were a few degrees warmer or cooler when ingested.

OTHER DRUGS

Coffee, tea, and chocolate (all of which contain caffeine) are commonplace refreshment drinks in urban settings, but no one in Peru thinks of them as drugs, and they are generally unimportant economically. In some parts of the eastern lowlands, the same is true of mate, or "Jesuit tea," which is brewed from *Ilex spp.*

As is true throughout much of the world, the most impoverished people in Peru often resort to mass-produced substances for relatively inexpensive (and physically dangerous) mind-altering experiences. The sniffing of gasoline, glue, dry-cleaning fluid, and other solvents and volatile chemicals takes a toll on many young people who roam in gangs through the streets of urban slums. As important as such behaviors may be to those who participate, however, they have little significance at the national level.

At the middle and upper levels of society, it is similarly not uncommon for some people to use prescription drugs or "designer" drugs to alter their consciousness. A few ethnographic studies show that such experiences differ little from those in other countries, but there are virtually no epidemiological data available.

POLICIES AND INTERNATIONAL RELATIONS

Social and cultural contexts tell more about the importance of drugs than do the experiences of individual users. Coca and *chicha* figured prominently in trade and political alliances in pre-Columbian times, just as cocaine does today. Both Spanish colonial and republican governments displayed an ambivalence about alcohol and coca by alternating prohibitions with permissiveness (especially with respect to the "Indian" or native population). As is often the case in other countries, Peru has many laws and regulations that are supposed to reduce both the use of drugs and the problems that arise from their excessive use. But enforcement is sporadic, highly personalized, and influenced by political and economic corruption.

There is widespread resentment that members of the U.S. Drug Enforcement Agency and armed forces are actively involved in attempts to curb the growing and processing of coca. The widespread use of herbicides harms people, livestock, and other crops, and interference with the drug traffic is seen as economic oppression, an insult to national sovereignty, and an immediate danger to the lives and property of those few Peruvians who are involved. In the 1980s and 1990s the Maoist guerilla group Sendero Luminoso (Shining Path) consistently defended the peasantry who were growing and processing coca. This activity won popular support for the guerilla movement, even those who did not share their extreme leftist ideology.

In sum, drug use has a long and honored tradition in many of the varied populations that comprise contemporary Peru, and it plays integral and varied roles in their cultures. Drug abuse is rare, however, and the problems that are associated with drugs more often stem from outside influences, misunderstandings, and heavy-handed restrictive policies than from the drugs or their traditional uses.

See also **Brazil; Colombia; Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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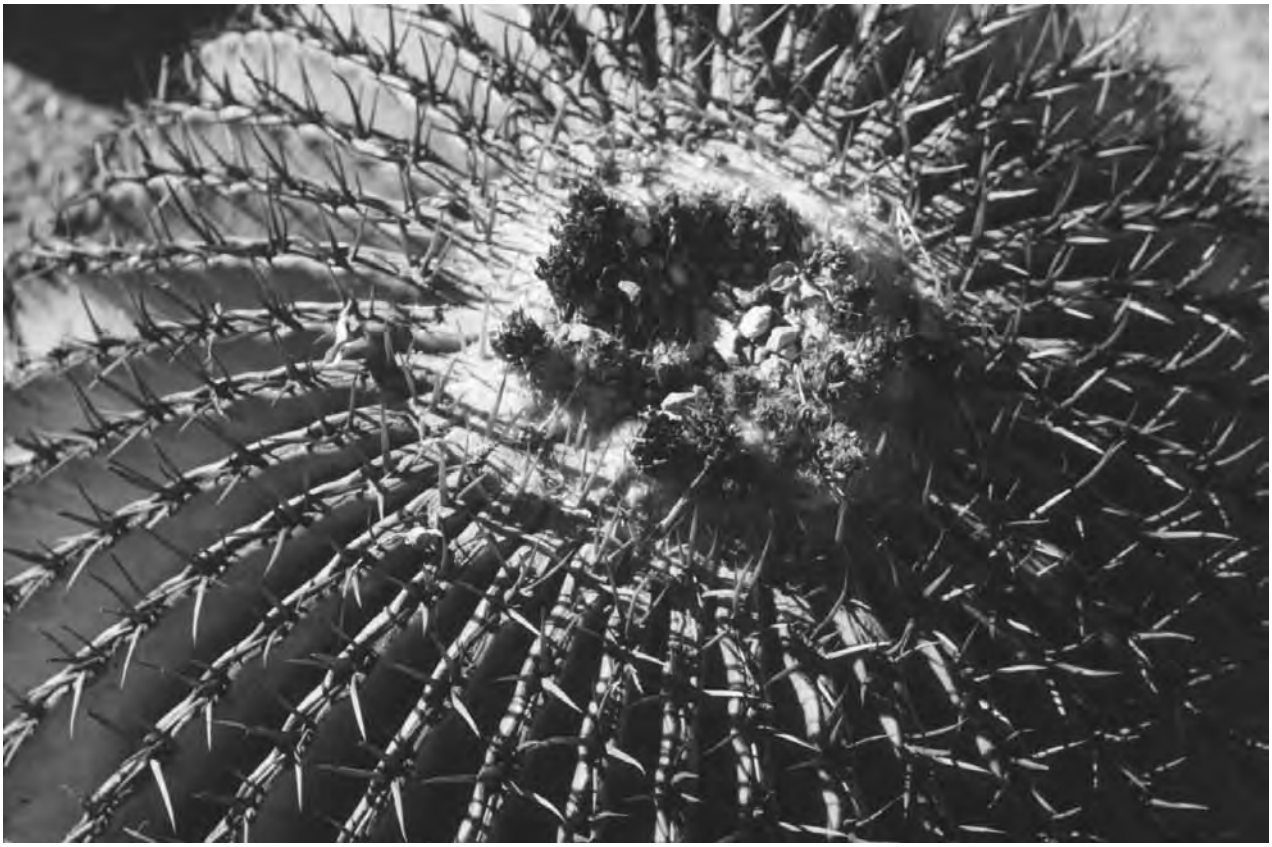
DWIGHT B. HEATH

PEYOTE. Peyote (or peyotl) is the common name for the cactus *Lophophore williamsii* or *Anhalonium lewinii*, which is found in the southwestern United States and northern Mexico. Although there are many compounds found in the cactus, some of which may be psychoactive, the principal hallucinogenic substance found in peyote is mescaline. As the other psychoactive substances may make some contribution to the psychedelic experience, there may be some slight difference in the behavioral effects produced by taking peyote and pure mescaline, but the overall effects of peyote are very similar to those produced by mescaline.



Peyote cactus, close-up, showing some small ''buttons'' on top. CUSTOM MEDICAL STOCK PHOTO, INC. REPRODUCED BY PERMISSION.

Peyote, one of the oldest psychedelic agents known, was used by the Aztecs of pre-Columbian Mexico who considered it magical and divine. Its use spread to other Native American groups who used it to treat various illnesses, as a vehicle to communicate with the spirits, and in highly structured tribal religious rituals. For these rituals, the dried tops of the cactus—the buttons—are chewed or made into a tea. Since peyote may cause some initial nausea and vomiting, the participant may prepare for the ceremony by fasting prior to eating the buttons. Peyote is usually taken as part of a formalized group experience and over an extended period of time; the peyote ceremonies may take place at night and around a communal fire to increase the hallucinogenic effects and visions.

See also **Ayahuasca; Dimethyltryptamine (DMT); Psilocybin.**

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DANIEL X. FREEDMAN
R. N. PECHNICK

PHARMACODYNAMICS. The study of the mechanism of how drugs act on the body is called pharmacodynamics. Most (but not all) drugs exert their action by binding to specific receptors. This binding may initiate changes that lead to the characteristic effects of the drug on body functions. An agonist is a drug that mimics the action of an endogenous ligand (e.g., a neurotransmitter or hormone) at a receptor. If various concentrations of an agonist are administered, the dose-response curve (see Figure 1) will show increased effects as one goes from left (low concentration) to right (high concentration). A full agonist is a drug that produces the maximal response. A partial agonist is a drug that provokes a response that is less than maximal. An antagonist is a drug that does not provoke a response by itself but that blocks agonist-mediated responses. An inverse agonist produces a response that is the opposite of the effect induced by an agonist.

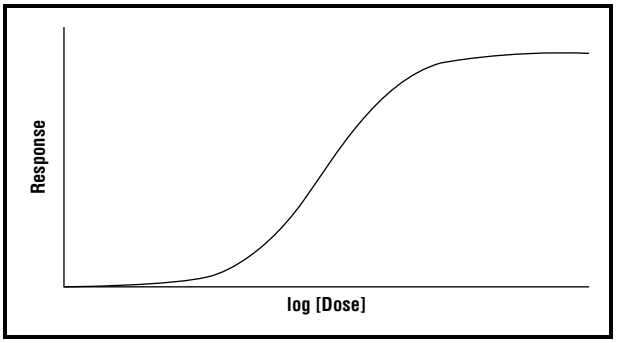

Figure 1. The shape of the dose-response curve. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

A central question in drug therapy is identifying the proper dose of the drug that will produce a desired action without many harmful side effects. To clarify this problem, pharmacologists analyze the relationship between dose and response, in which the X-axis shows the concentration of a drug or a hormone and the Y-axis shows the response to the drug or hormone, which could be almost any type of measure. Most dose-response curves are sigmoidal (shaped like an S). The log-dose-response can be viewed as having four parameters: potency, slope, maximal efficacy, and variability. Potency describes the strength of drug effects. It is usually employed to calculate relative strengths among drugs of the same class. Slope refers to the central part of the curve that is approximately straight. It is used to analyze drug concentration (dose) from the observed corresponding responses. Maximal efficacy, or simply efficacy, is the greatest effect produced by the drug. This is one of the major characteristics of a drug. Efficacy and potency of a drug are not necessarily correlated, and the two characteristics should not be confused.

Many drugs, including drugs of abuse, produce tolerance, that is, it becomes necessary to take progressively larger doses to achieve the same drug effect or the same dose has a reduced effect. Sensitization involves the increase in the strength of a response to a stimulus induced by past experiences with the same or related stimuli. This increase represents adaptation, making

the drug effect easier to elicit on future occasions. In some cases, the brain and other tissues on which a drug acts undergo adaptive changes (neuroadaptations) that tend to offset the drug effect. When a drug that produces neuroadaptation is withdrawn, the brain and other tissues have to readapt because they are no longer balanced by the drug effect. The adaptation produces a variety of signs and symptoms called the *withdrawal syndrome*. The severity of this syndrome depends on the degree of adaptive changes in the nervous system which, in turn, depends on the dose and the duration of exposure to the drug. The particular characteristics of the withdrawal syndrome depend on the pharmacological effects of the drug(s) and typically are opposite to the drug effects. For example, morphine constricts the pupil; the morphine withdrawal syndrome includes pupillary dilation.

Most drugs of abuse produce pleasant effects in humans. For example, some people use amphetamines or other stimulants (e.g., cocaine) to achieve a sense of well-being and euphoria. Some people use depressants—alcohol, opioids, or tranquilizers—to relax. Still others use either stimulants or depressants to relieve boredom or reduce anxiety or pain. The common feature is that people use drugs because somehow the drug is rewarding to the user, either by producing a feeling of well-being (e.g., euphoria, elation) or by taking away a negative feeling (e.g., anxiety).

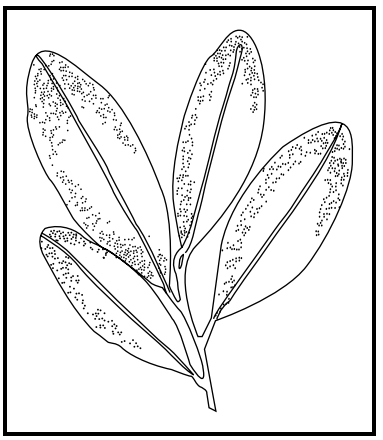

Figure 2. Coca leaf. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

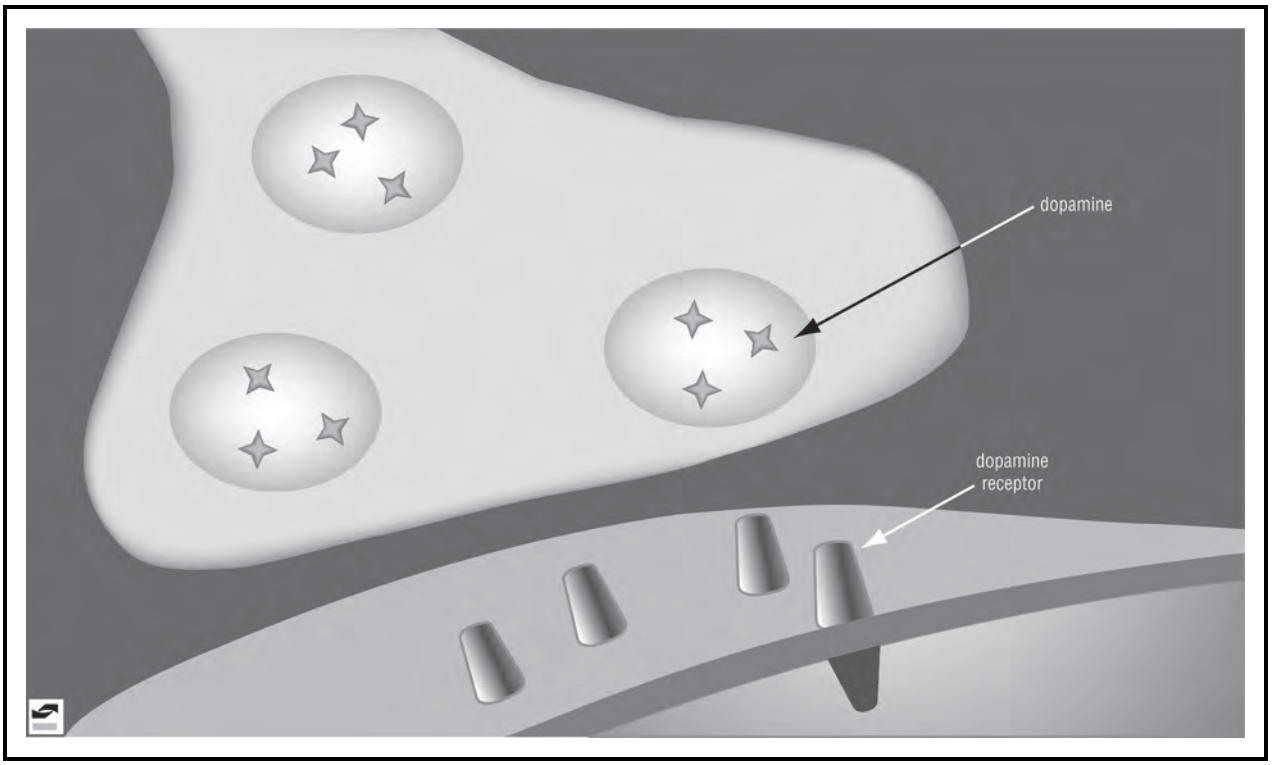

Figure 3. Dopamine neurotransmission. (Source: NIDA Notes, Vol. 13, No. 5, Feb. 1999. National Institute of Drug Abuse, National Institutes of Health, U.S. Department of Health and Human Services.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

An extensive literature defines the role of dopamine (DA) in the motivational, rewarding and reinforcing effects of all drugs of abuse (Volkow et al., 2007). Alcohol, for example, activates DA release in the nucleus accumbens and surrounding extended amygdala (Heimer et al., 1997; Lyness et al., 1992; Weiss et al., 1993). The action of alcohol on the mesolimbic dopaminergic reward pathway is strongly associated with susceptibility to alcoholism (Noble, 1996); the development of craving and loss of control (Robinson & Berridge, 1993); and the acquisition of excessive motivational properties by alcohol-related cues. Brain dopaminergic systems are highly complex, with at least seven receptor subtypes, though most research has examined D2 dopamine receptors. Reduced levels of DA and of D2 receptors have been found in alcohol-preferring (*P*) rats during alcohol withdrawal. DA levels in *P* rats rise when the animals anticipate receiving alcohol (Weiss et al., 1992). Imaging studies in alcoholics also show a lower density of D2 receptors (Volkow et al., 2002a; Volkow et al., 2002b). The density of D2 receptors is also modulated by environmental factors (e.g., social hierarchy in monkeys; Morgan et al., 2002), suggesting that strategies could be developed to increase the expression of D2 receptors (Volkow et al., 2002c). Administration of a viral vector to deliver the gene encoding the D2 receptor to *P* and alcohol-non-preferring (*NP*) rats resulted in the overexpression of D2 receptors and a significant reduction in alcohol intake (Thanos et al., 2001). Imaging studies have shown that activation of DA in limbic and memory circuits (amygdala, dorsal striatum, and hippocampus) may contribute to craving, which can be associated with relapse in abstinent alcoholics (Volkow et al., 2002c). Increased D2 receptor activity was found in unaffected siblings of alcoholics, suggesting a protective effect of increased dopaminergic activity (Volkow et al., 2006). Furthermore, studies have shown that the high associated with cocaine results not only from the absolute increase in DA concentration but also from the rate at which DA increases. The faster the increase of DA, the more intense the reinforcing effects are (Volkow et al., 2007). Brain imaging studies show that in subjects dependent on cocaine there is a down-regulation (decrease) in D2 receptor density and of DA release in the nucleus accumbens, the reward center of the brain. Each of these decreases in function contributes to decreased sensitivity to naturally occurring rewards. The decreased sensitivity of reward circuits would lead to decreased interest in common environmental stimuli, possibly predisposing individuals to seek drug stimulation as a means to activate these reward circuits and forming the foundation of the transition from using cocaine (and other addictive drugs) to feel high to taking cocaine to feel normal. Cocaine, like other drugs, is much more potent in stimulating DA-regulated reward than are natural reinforcers; but unlike natural reinforcers, drugs are able to activate down-regulated circuits (Volkow et al., 2007). However, even addicting drugs have limited effectiveness, and a continual decrease in normal DA function could underlie the development of tolerance and the subsequent need to increase the dose of a drug such as cocaine to activate sufficient DA release from down-regulated reward center circuits.

See also **Receptor, Drug; Tolerance and Physical Dependence.**

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PHARMACOKINETICS: GENERAL.

Pharmacokinetics describes quantitatively what the body does to drugs, including their absorption, distribution throughout the body, metabolism, and ultimate elimination. The rates of these processes are important in characterizing the fate of a medication in the body.

The actual percentage of a drug contained in a drug product that enters the circulation unchanged after its administration, combined with the rate of entry into the body, determines the bioavailability of a drug.

Once absorbed, most drugs are carried from their site of action and elimination by the circulating blood. Some drugs simply dissolve in serum water but many others are carried bound to proteins, especially albumin. Plasma protein binding influences the fate of drugs in the body, since only the free (unbound) drug reaches the site of drug action. This interaction with binding sites is reversible.

The intensity of drug action is most frequently related to the concentration of the drug at the site of action. The duration of drug effect is related to the persistence of its presence at this site. The time to reach maximum drug concentrations (or peak effects) is usually referred to as *tmax.*

Whenever the fate of a drug in the body is described by pharmacokinetic parameters, a model of the body is assumed. The fundamental principles of pharmacokinetics are based on the most elementary model. The body is considered a single compartment. Distribution of the drug is considered uniform. The volume in which the drug is distributed is referred to as the *volume of distribution* (Vd). It is typically expressed in liters per kilogram (L/kg).

Elimination of the drug is assumed to be exponential. The rate of elimination of a drug is usually described by its *half-life* ($t_{1/2}$), which is the time required for 50 percent elimination of the drug. This is typically expressed in hours (h). Another way to express drug elimination, and the most important pharmacokinetic parameter, is called clearance, which is the volume of plasma blood from which a drug is completely removed per unit time. The amount eliminated is proportional to the concentration of the drug in the plasma/blood. Clearance is usually expressed in milliliters per minute per kilogram (ml/min/kg) but can also be expressed in liters per hour per kilogram (L/h/kg).

An effect of a single dose of a drug may be characterized by its latency, the time needed for drug concentrations to reach maximum levels (tmax). Magnitude of peak effects and duration of action dosage and rates of absorption and

Drug	Dosage/route (mg)	Bioavailability (F) (%)	Protein binding (%)	t_{max} (h)	Mean $t_{1/2}$ (h) (range)	Vd (L/kg)	Cl (ml/min/kg)
Butorphanol	2/IV	100 (IM)	80	0.75	3–4	5	385
Codeine	60 oral/TIV	40–80 (oral)	7–53	1	3 (2.3–9.3)	2–6	15
Dextromethorphan		>50 (oral)	30–50	—	2–3 (estimated)	3–5	—
Heroin (3,6 diacelylmorphine) (see morphine)							
Buprenorphine	4–16/IV	79 (oral)	—	—	3.0 minutes	—	31
	0.3/IV	40–90 (oral)	—	—	2–3	1–3	900–1,200 (ml/min)
Pentazocine	—	47 (oral)	65	—	4.5	7	17
Morphine	0.01/mg/kg	15–64 (oral)					
		100 (IM)	35	<1	2–4	3–4	12–21
		48 (rectal)					
		2 (epidural)					
Methadone	15–80	92 (oral)	40	<1	25 (13–47)	3.8	1.4
Meperidine	50–100/IM	50–60 (oral)	50–60	—	3–4	3–5	—
Propoxyphene	130	40–90 (oral)	—	1–2	2–15	—	—
Nalbuphine	—	16 (oral)	—	1–2	2–3	3–4	22
Naltrexone	—	5–40 (oral)	20	—	2–3	19	48

Vd = Volume of distribution
Cl = Clearance
IV = Intravenous
IM = Intramuscular

Table 1. Pharmacokinetic parameters of opioids. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Drug	Dosage/route (mg)	Bioavailability (F) (%)	Protein binding (%)	t_{max} (h)	Mean $t_{1/2}$ (h)(range)	Vd (L/kg)	Cl (ml/min/kg)
Amphetamine	15–25/oral	—	23–26	1.25	14 (2–22)	6.1	0.2–0.6 (L/min)
Caffeine	1–5 mg/kg/oral	100 (oral)	15–40	0.5–1	5 (1–10)	0.6	1
Cocaine	30–100/IV;IN	28–51 (IN)	7	0.5–1.5	(0.3–1.5)	2	11
Nicotine	0.25–2 (mg/kg/min)/IV	30	5	—	2 (0.8–3.5)	1–2	18

Vd = Volume of distribution
Cl = Clearance
IV = Intravenous
IN = Intranasal

Table 2. Pharmacokinetic parameters of stimulant drugs. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

elimination are influenced by these parameters. As dosage increases, latency is reduced and peak effect increased without a change in the time of peak effect. Reduced elimination (long half-life, reduced clearance) results in an expected prolongation of drug effects and in some cases drug accumulation. Using more complex models than a single compartment model, physicians use pharmacokinetic data not only to characterize the fate of a drug in the body but also to calculate doses and frequency of drug administration for each particular patient. This determination is important because there are wide variations among individuals in the absorption, distribution, and elimination of drugs.

Tables 1 through 4 summarize the available data on the kinetic properties of alcohol and other abused drugs. Some of the drugs of abuse included in this summary are illicit drugs (e.g., cocaine), whereas others are therapeutic agents that have the potential for abuse (e.g., opioids).

Although some of the drugs included in the tables have been used for centuries (e.g., alcohol, caffeine), knowledge of their kinetics and metabolism

Drug	Dosage/route (mg)	Bioavailability (F) (%)	Protein binding (%)	t_{max} (h)	Mean $t_{1/2}$ (h) (range)	Vd (L/kg)	Cl (ml/min/kg)
Alcohol (ethanol)	—	80 (oral)	—	<1	0.25	0.5	124 mg/kg/h
Alprazolam	0.5–30/oral	90 (oral)	70	0.7–1.6	12 (6–18)	0.7–1.5	0.7–1.3
Bromazepam	0.25–3/oral	—	70	1	10–15	—	—
Chlordiazepoxide	20–50/oral IV, IM	100 (oral) PO or (IM)	95	0.5–3	10 (6–28)	0.3	0.5
Clobazam	10–20/oral	Good (oral)	90	1.3–1.7	25 (16–49)	0.9–1.8	0.36–0.63
Clonazepam	—	98	86	1–2	23 (20–80)	3.2	1.55
Clorazepate (see Desmethyldiazepam)	—	—	—	—	2.0	0.33	1.8
Desalkylflurazepam	—	—	—	1	75 (40–200)	22	4.5
Desmethyldiazepam	—	99	97	1–2	51 (51–120)	0.78	0.14
Diazepam	1–40/oral IM, IV	100 (oral) 50–60 (IM, rectal)	96	0.5–2	31 (14–61)	1 (0.9–3.0)	0.38–0.51
Flurazepam (see Desalkylflurazepam)	15–90/oral	—	97	—	—	—	—
Halazepam (see Desmelhyldiazepam)	—	—	—	—	—	—	—
Lorazepam	2–4/oral	93 (oral) 90 (IM)	90	1.5	13 (8–25)	0.8–1.6	1 (0.8–1.3)
Midazolam	5–15/oral IV, IM	44 (oral)	95	0.3–0.7	2 1.4–5	0.8–17	6
Nitrazepam	15–30/oral	78 (oral)	87	2	26 (16–48)	1.2–2.7	0.86
Oxazepam	15–45/oral	97 (oral)	98	3 (0.5–8)	7 (5.1–13)	0.5–2.0	0.6–2.9
Prazepam (see Desmethyldiazepam)							
Temazepam	10–30/oral	>80 (oral)	98	0.8–4.7	12 (7–17)	1.3–1.5	1.0–3.4
Triazolam	0.25–1.0/oral	44 (oral) 53 s.l.	90	1.6	2.5 (2–5)	1.1	3.7–8.8

Vd = Volume of distribution
Cl = Clearance
IV = Intravenous
IM = Intramuscular
s.l. = Sublingual

Table 3. Pharmacokinetic parameters of central nervous system depressants. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Drug	Dosage/route (mg)	Bioavailability (F) (%)	Protein binding (%)	t_{max} (h)	Mean $t_{1/2}$ (h) (range)	Vd (L/kg)	Cl (L/min)
Marijuana (Δ^9-tetrahydrocannabinol)	0.5–30	8–24 (smoked) 4–12 (oral)	95–26	3–8 min	25 (19–57)	626(L)	0.2–1
Phencyclidine (PCP)	0.1–0.7/IV Inhaled	5–90	65	1.5	24 (7–51)	6.8	0.30 (0.14–0.77)

Vd = Volume of distribution
Cl = Clearance
IV = Intravenous

Table 4. Pharmacokinetic parameters of hallucinogens. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

is recent and in some cases still incomplete. This lack of information is due partly to their complex metabolism and partly to the difficulties of studying drugs of abuse in humans.

The tables show the route of administration, the type of subjects used in the study, the doses used, and the most important kinetic parameters, such as protein binding, half-life, volume of distribution, and clearance.

See also **Pharmacokinetics of Alcohol.**

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PHARMACOKINETICS: IMPLICATIONS FOR ABUSABLE SUBSTANCES.

Pharmacokinetics is the study of the movements and rates of movement of drugs within the body, as the drugs are affected by uptake, distribution, binding, biotransformation, and elimination. An understanding of the biological basis of the clinical actions of abused drugs depends, in part, on knowledge of their neurochemical and neuroreceptor actions that reinforce and sustain drug use (Hall et al., 1990). The pharmacokinetic properties of

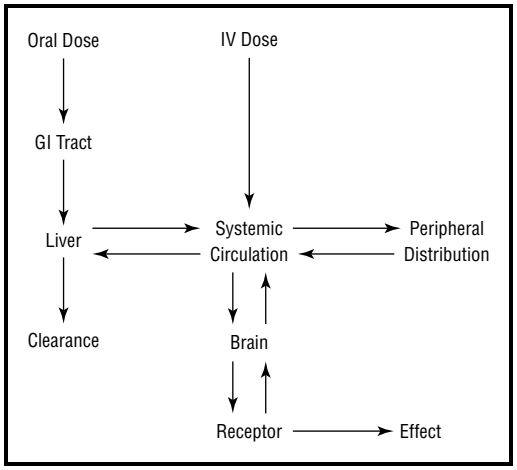

Figure 1. Schematic representation of physiological and pharmacokinetic events. These occur between administration of a centrally acting compound and the production of a pharmacological effect. If the medication is given orally, it must pass from the gastrointestinal (GI) tract to the portal circulation and to the liver before reaching the systemic circulation. Intravenous administration, however, yields direct access to the systemic circulation. Drugs of abuse may be taken by the intravenous route but are also taken by intranasal, intrabuccal, rectal, or inhalational routes, all of which will avoid the initial gastrointestinal-portal–hepatic exposure. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

abusable substances represent a second important component of the database. The discipline of pharmacokinetics applies mathematical models to explain and predict the time course of drug amounts (doses) and their concentrations in various body fluids (Greenblatt, 1991, 1992; Greenblatt & Shader, 1985). Pharmacokinetic principles can be used to provide quantitative answers to questions involving the relationship of drug dosage and route of administration to the amount and time course of the drug present in systemic blood and at the receptor site of action.

Before an orally administered psychoactive drug can exert a pharmacological effect through its molecular recognition site in the brain, a number of events must take place (see Figure 1). The drug must reach the stomach and dissolve in gastric fluid. The stomach empties this solution into the proximal small bowel, which is the site of absorption of most medications. The drug must diffuse across the gastrointestinal mucosal barrier, reach the portal circulation, and be delivered to the hepatic (liver) circulation. (The liver detoxifies chemicals, including drugs.) Before reaching the systemic circulation, then, the absorbed drug must survive this initial exposure to the hepatic circulation, sometimes termed the *first-pass* through the liver (Greenblatt, 1993). After reaching the systemic blood, the drug is transported to the cerebral (brain) capillary circulation as well as to all other sites in the body that receive blood directly from the heart (cardiac output). The drug diffuses out of the cerebral capillary circulation, crosses the lipoidal (fatty) blood-brain barrier, and reaches the extracellular water surrounding the neuroreceptor site of action. Only then is the drug available to interact with its specific molecular recognition site.

All of these processes take time, and some may serve as obstacles that delay or prevent the drug from reaching its site of action. Pharmacokinetic models incorporate the physiology of these processes and can allow rational assessment of important clinical questions: How much drug reaches the brain? How fast does it get there? How long does it stay there?

DRUG ABSORPTION

The term *lag time* refers to the time that elapses between ingestion of an oral medication and its first appearance in the systemic circulation (see Figure 2). For most drugs, it generally falls between 5 and 45 minutes. For ethanol (drinking alcohol, which is also called ethyl alcohol), however, the lag time may be very short because the drug is already a liquid at the time it is ingested, and a significant component of absorption probably occurs across the gastric mucosa as well as in the proximal small bowel (Frezza et al., 1990). The physicochemical features of the drug contribute importantly to the time necessary for dissolution and, therefore, to the lag time. All else being equal, drugs in solution have shorter lag times than those administered in suspension form; they are, in addition, more rapidly absorbed than capsule preparations, tablet preparations and, finally, preparations intended to be used rectally. For any given solid dosage form, lag time and absorption rate are likely to be shorter if the drug particles are more finitely subdivided. Sustained-release (time-release) drug formulations are deliberately prepared to have long lag times and slow absorption rates, thereby avoiding drug effects associated with the peak concentration.

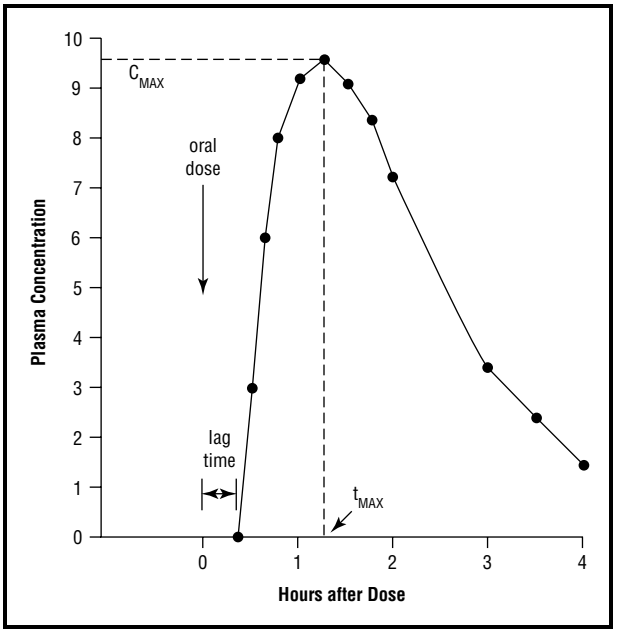

Figure 2. Schematic plot of plasma concentration versus time after oral dosage (given at time zero [arrow]). A lag time elapses between the time of administration and the beginning of appearance in the systemic circulation. Plasma levels then rise, reach a peak, and fall: c_{max} is the peak plasma concentration (9.6 units) and t_{max} is the time of peak concentration (1.25 hours after dosage). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Absorption rate refers to the time necessary for the drug to reach the systemic circulation once the absorption process actually begins. Pharmacokinetic models can be applied to assign a half-life value to the process of absorption. Values of absorption half-life tend, however, to be of low statistical stability, and it is increasingly common to characterize the absorption process using the observed peak plasma concentration (cmax) and time of peak concentration (tmax). The tmax is actually a composite of the lag time plus the time necessary to reach peak concentration once absorption starts (Figure 2). In general, fast absorption implies a high value of cmax and a short value of tmax; slow absorption implies a long tmax and a low cmax. Again, sustained-release drug preparations are deliberately formulated to produce long lag times and slow absorption, thereby delaying and reducing the cmax after an oral dose. Drug absorption tends to be slower when medications are taken during or just after a meal, rather than in the fasting state (before a meal, on an empty stomach).

For these reasons, the ethanol in alcoholic beverages is relatively rapidly absorbed after oral ingestion. The popular lore that alcohol has a greater effect when taken on an empty stomach probably has a physiological basis, since peak concentrations are higher and earlier when alcohol is taken in the fasting state. Benzodiazepine derivatives (tranquilizers) clearly are not primary drugs of abuse and are seldom subject to misuse by the great majority of patients; however, benzodiazepines may be taken for non-therapeutic purposes by some substance abusers (Woods, Katz, & Winger, 1987, 1992; Shader & Greenblatt, 1993). The preference of specific benzodiazepines by drug abusers appears to be closely related to their rate of absorption. That is, rapidly absorbed benzodiazepines, leading to relatively high values of cmax shortly after dosage, appear to be preferred by drug abusers. The benzodiazepine diazepam (Valium), for example, is much more rapidly absorbed than is oxazepam (Serax or Serenid). In controlled laboratory settings, diazepam is more easily recognized as a potentially abusable substance by experienced drug users, and it is also preferred by this group to oxazepam (Griffiths et al., 1984a, 1984b). This preference also appears to be supported by epidemiological studies of prescription drug misuse (Bergman & Griffiths, 1986).

Some orally administered medications reach the systemic (blood) circulation in small or even negligible amounts relative to the dose ingested. Incomplete absorption from the gastrointestinal tract sometimes explains this. However, oral medications may be poorly available to the systemic circulation even if they are well absorbed. This is explained by the phenomenon termed *presystemic extraction*, which results from the unique anatomy and physiology of the gastrointestinal circulation (Greenblatt, 1993). Orally administered medications are absorbed into the portal rather than systemic circulation (Figure 3), and portal blood drains directly into the liver. Many drugs that are avidly metabolized in the liver may, therefore, undergo substantial biotransformation before reaching systemic blood. Some drugs may also be metabolized by the gastrointestinal (GI) tract mucosa. First-pass hepatic metabolism together with GI tract metabolism is collectively termed *presystemic extraction*. Cocaine, for example, is not favored as a drug of abuse by the oral route because of nearly complete presystemic extraction, allowing only small amounts of the intact drug to reach the systemic circulation (Jatlow, 1988; Jeffcoat et al., 1989).

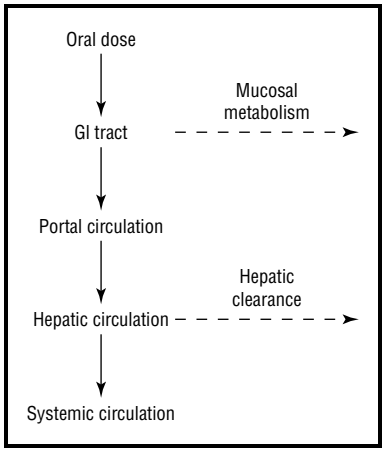

Figure 3. Possible mechanisms of presystemic extraction. Orally administered medications may undergo metabolism as they pass through the gastrointestinal tract mucosa (dashed arrow), which contains significant amounts of Cytochrome P45-3A4. Mucosal metabolism of cyclosporine appears to occur in humans (Kolars et al., 1991). Metabolism may also occur as the drug present in portal blood passes through the hepatic circulation (dashed arrow); this is termed "first-pass" metabolism. The net extent of presystemic extraction depends on the combination of mucosal metabolism and first-pass metabolism. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

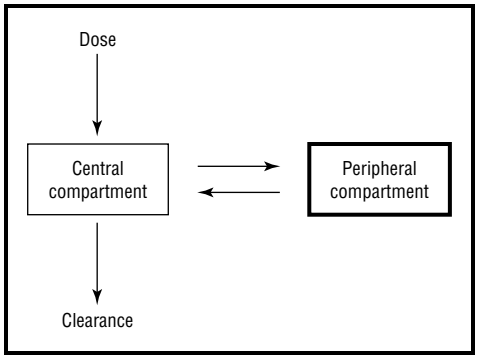

Figure 4. Schematic diagram of the Two-Compartment Model. It is assumed that medications are administered into and cleared from the central compartment only, and that only the central compartment (which includes blood) is accessible to measurement. Reversible distribution occurs between central and peripheral compartments. For most psychotropic drugs, high lipid solubility favors distribution to the peripheral compartment, producing a large apparent pharmacokinetic volume of distribution. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

DRUG DISTRIBUTION

The process of distribution is an important determinant of pharmacokinetic properties, as well as the time course of action, of most centrally acting drugs, including those that are subject to abuse. Drugs reversibly distribute not only to their site of action in the brain but also to peripheral sites such as adipose (fat) tissue and muscle, where they are not pharmacologically active (Figure 1). Only a small fraction of the total amount of a psychotropic drug in the body goes to the brain. An even smaller fraction actually binds to the specific molecular recognition site (receptor). The extent of distribution of a psychotropic drug is determined in part by lipid (fat) solubility (how well a substance dissolves in oils and fats; lipophilicity), which is related to molecular structure and charge. Most psychotropic drugs are highly lipid-soluble. Drug distribution is also determined by some characteristics of the organism: the relative amounts of adipose and lean tissue, blood flow to each individual tissue, and the extent of drug that binds to plasma protein. The overall extent of drug distribution throughout the body can be quantified by the pharmacokinetic volume of distribution, which is a ratio: the total amount of drug present in the body divided by the concentration in a reference compartment, usually serum or plasma. Lipid-soluble psychotropic drugs, as well as drugs of abuse, typically have very large pharmacokinetic volumes of distribution, which may exceed body size by tenfold or more. Although the drug cannot actually distribute to a space larger than the body, low plasma concentrations resulting from extensive uptake into peripheral tissues can yield a large apparent pharmacokinetic volume of distribution (Figure 4).

Drug distribution influences both onset and duration of drug action, as well as the observed value of elimination half-life. After an intravenous (IV) injection, lipid solubility allows for the rapid crossing of the lipoidal blood-brain barrier, leading to a rapid onset of pharmacological action (drug effect). In behavioral terms, then, drug-taking produces immediate reinforcement. The duration of a drug's action, however, is determined mainly by the extent of its peripheral distribution. Plasma levels of lipid-soluble psychotropic drugs will decline rapidly and extensively after a single intravenous dose because of peripheral distribution rather than elimination or clearance (Figure 5). A similar principle holds after oral administration of rapidly absorbed drugs (De Wit & Griffiths, 1991). Since duration of action after a single dose is determined more by distribution than by elimination or

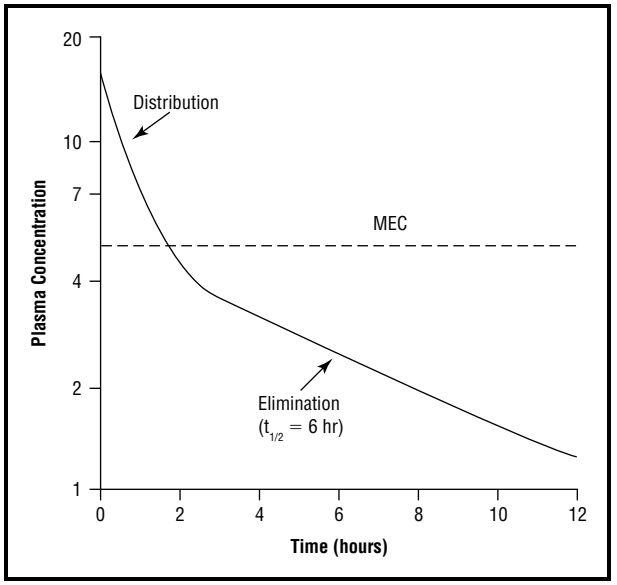

Figure 5. Plasma concentrations of a hypothetical lipid-soluble drug after intravenous injection. Disappearance from plasma is biphasic. The initial rapid phase is mainly due to drug distribution from central to peripheral compartments (see Figure 4). The slower phase of elimination is mainly due to clearance. For this drug, the elimination half-life in the postdistributive phase is 6 hours. If a plasma concentration of 5 units represents the minimum effective concentration (MEC) below which the drug exerts no detectable pharmacological effect, this drug in the dosage administered has a duration of action of approximately 2 hours. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

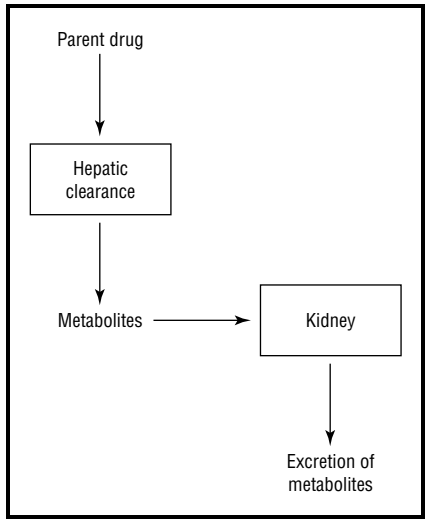

Figure 6. Psychotropic drugs: Most, including drugs of abuse, are cleared via the liver by hepatic biotransformation to metabolic products. The metabolites may then be released into the circulation and excreted by the kidney. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

clearance, it is generally not accurate to equate elimination half-life and duration of action.

CLEARANCE AND ELIMINATION

The terms *clearance* and *elimination half-life* are commonly used to describe the bodily process of drug removal or disappearance. These two concepts are related but are not identical. Clearance is the most important, since it is a unique independent variable that best describes the capacity of a given organism to remove a given drug from its system. Clearance has units of volume divided by time—for example, milliliters/minute (ml/min) or liters/hour (L/h)—and is the total amount of blood, serum, or plasma from which a substance is completely removed per unit of time. Clearance is not identical either to the rate of drug removal or to the elimination half-life. For most psychotropic drugs, clearance is accomplished by the liver via processes of biotransformation that change the administered drug into one or more metabolic products (Figure 6); this is commonly called *detoxification* by the liver. The metabolites may appear in the urine, but the liver is still the organ that affects clearance. For drugs cleared exclusively by the liver, the numerical value of clearance cannot exceed hepatic blood flow.

Elimination half-life is described in units of time; it can be seen as the time necessary for the plasma concentration to fall by 50 percent after distribution equilibrium has been attained. The elimination phase of drug disappearance—at which time the concept of elimination half-life is applicable—may not be attained until completion of an initial phase of rapid drug disappearance resulting from peripheral distribution (see Figure 5). As discussed earlier, the duration of action of a single dose of a psychotropic drug is not necessarily related to its elimination half-life.

Pharmacokinetic theory yields the following relationship between a drug's elimination half-life, volume of distribution (Vd), and clearance: Elimination half-life = 0.693 × Vd ÷ clearance. The independent variables, appearing on the right side of the equation, are Vd, the physicochemically determined property reflecting the extent of

Parent drug	Urinary metabolite
Marijuana (Tetrahydrocannabinol, THC)	11-nor-delta-9-THC-9-carboxylic acid
Cocaine	Benzoylecgonine
Heroin	Morphine glucuronide

Table 1. Principal urinary metabolites of potentially abusable drugs. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

distribution, and clearance, having units of volume divided by time, quantifying the capacity for drug removal. Elimination half-life is dependent on both of these. Note that a drug may have long elimination half-life, due either to a large Vd, a low clearance, or both.

PHARMACOKINETICS VERSUS PHARMACODYNAMICS

In contrast to pharmacokinetics or how the body acts on a drug, pharmacodynamics is the quantitative study of the time course of how a drug acts on the body. If drug distribution to the site of action occurs by passive diffusion from the systemic circulation, and if the intensity of drug action depends on the degree of receptor occupancy both in time and in quantity, then pharmacokinetics and pharmacodynamics are necessarily related. Kinetic-dynamic modeling, discussed in detail elsewhere (Greenblatt & Harmatz, 1993), addresses this relationship mathematically, by directly evaluating concentration versus effect. In the fields of psychopharmacology and substance abuse, kinetic-dynamic modeling is a major challenge, since (1) clinical drug effect (pharmacodynamic response) often is difficult to measure reliably and since (2) measured drug concentrations in systemic serum or plasma do not always parallel those at the central site of action. Nonetheless, certain advances in kinetic-dynamic modeling have significantly advanced the understanding of the relationship of the pharmacokinetics of psychotropic drugs to their pharmacodynamic effects.

ALTERED PHARMACOKINETICS ALTERS PHARMACODYNAMICS

Metabolic (i.e., pharmacokinetic) changes can result in changes in drug action. For example, differences in slow versus rapid metabolism can contribute to differences in dosing requirements and the need for lower or higher doses (LaLovic et al., 2004). For example, Cytochrome P450 2D6 (CYP2D6) is a polymorphic enzyme that metabolizes many analgesics, antipsychotics, and antidepressants. Approximately 7 percent of Caucasians and 1 to 3 percent of other populations lack this enzyme and are classified as poor metabolizers (PMs). Poor metabolizers require lower dosages of a drug to achieve a therapeutic effect. Approximately 1 to 7 percent of European Caucasians have multiple copies of the gene and thereby produce more of this enzyme. These individuals are classified as ultrarapid metabolizers (UMs). The prevalence of UMs appears to be higher in some populations such as Saudi Arabians (20%) and Ethiopians (29%). When UMs are treated with typical doses of tricyclic antidepressants, for example, they have very low plasma concentrations and do not respond to the treatment. Codeine, hydrocodone, and oxycodone are activated by CYP2D6 (with codeine being converted to morphine by CYP2D6). Therefore, if the CYP2D6 enzyme is missing or inhibited by another drug such as paroxetine or fluoxetine, codeine does not work as an analgesic. Additionally, CYP2D6 PMs appear to be protected from dependence on these oral opioids (De Leon et al., 2003).

Physical changes in pharmacokinetics can also result in altered pharmacodynamics. For example, OxyContin tablets are designed to provide controlled delivery of oxycodone over 12 hours. Steady-state levels are achieved within 24 to 36 hours. OxyContin (10 mg) given every 12 hours compared to immediate-release oxycodone (5mg) given every 6 hours, are equivalent for area under the curve (AUC) and cmax, and similar for cmin (trough) concentrations. However, breaking, chewing or crushing OxyContin tablets eliminates the controlled delivery mechanism and results in the rapid release and absorption of the entire dose of oxycodone, potentially resulting in a fatal overdose of the drug. Additionally, because oxycodone is water soluble, crushed tablets can be dissolved in water and the solution injected. The rapid delivery of a large dose of oxycodone results in significant dopamine release in the nucleus accumbens via disinhibition of GABAergic control of the mesolimbic dopamine tract. Dependence occurs at least partially due to the rapid release of dopamine resulting in strong positive reinforcement and a disruption in allostasis (Koob & Le Moal, 2008). *Allostasis,* which means to maintain stability or homeostasis through

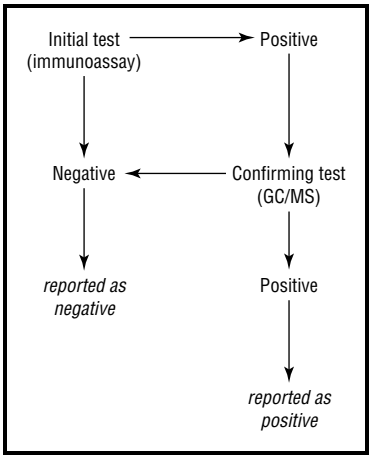

Figure 7. Urine-testing programs. Those for drugs of abuse typically use a two-tiered algorithm. An initial screening test is done with a relatively inexpensive, nonspecific, and insensitive immunoassay (such as enzyme-multiplied-, fluorescence-polarization-, or radio-immunoassay). If the initial test is negative, the result is reported as such, and no further testing is done. If the initial screen is positive, a second analysis is done on the same sample using a more accurate and specific method, such as gas-chromatography/mass-spectroscopy (GC/MS). If the confirmation test is negative, the result is reported as negative. If GC/MS confirms the initial screening test, the result is reported as positive. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

change, was introduced by Sterling and Eyer (1988) to describe how the cardiovascular system adjusts to resting and active states of the body.

As adapted by Koob and Le Moal (1997) for addiction, allostasis involves a continuous re-evaluation of drug need and re-adjustment of neurobiological mechanisms toward a new homeostasis. Oxycodone is well absorbed from OxyContin tablets with an oral bioavailability of 60 to 87 percent. The relative oral bioavailability of OxyContin to immediate-release oral dosage forms is 100 percent. This high oral bioavailability is due to low pre-systemic extraction. In normal volunteers, the half-life of absorption is 0.4 hours for immediate-release oral oxycodone. In contrast, OxyContin tablets exhibit a biphasic absorption pattern with two apparent absorption half-lives of 0.6 and 6.9 hours, which describes the initial release of oxycodone from the tablet followed by a prolonged release. When OxyContin is crushed or broken, individuals are at risk for overdose or death, as they receive a greater portion of the entire dose (e.g., 80 mg) due to increased bioavailability combined with a more rapid half-life. Oxycodone is extensively metabolized and is eliminated primarily in the urine as both conjugated and unconjugated metabolites. The elimination half-life of oxycodone following the administration of OxyContin is 4.5 hours compared to 3.2 hours for immediate-release oxycodone.

OxyContin is not indicated for rectal administration. OxyContin tablets administered rectally result in an AUC 39 percent that is greater and a cmax 9 percent that is higher than tablets administered orally. Therefore, there is an increased risk of adverse events with rectal administration. Oxycodone binding to plasma protein at 37°C and a pH of 7.4 is about 45 percent. Oxycodone hydrochloride is extensively metabolized to noroxycodone, oxymorphone, and their glucuronides. The major circulating metabolite is noroxycodone, which is a considerably weaker analgesic than oxycodone. Oxymorphone, although possessing analgesic activity, is present in the plasma only in low concentrations. The correlation between oxymorphone concentrations and opioid effects was much less than that seen with oxycodone plasma concentrations. The analgesic activity profile of other metabolites is not known. The formation of oxymorphone, but not noroxycodone, is mediated by cytochrome P450 2D6 and, as such, its formation can, in theory, be affected by other drugs. Oxycodone and its metabolites are excreted primarily via the kidney. The total plasma clearance was 0.8 L/min for adults.

A comprehensive approach to understanding the biological bases of substance abuse must combine the neurochemical and molecular mechanisms that underlie the behavioral effects of these drugs with an understanding of their properties of absorption, distribution, and clearance. Advances initially made in the 1980s continued to be made as research techniques in both disciplines became increasingly refined.

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PHARMACOKINETICS OF ALCOHOL. The discipline known as *pharmacokinetics* deals with the way drugs are absorbed, distributed, metabolized, and eliminated by the body and how these processes can be described in quantitative terms. The pharmacokinetics of alcohol (ethyl alcohol or ethanol) is an important issue in forensic toxicology and clinical medicine, when the amount of alcohol in the body is estimated from the concentration measured in a blood sample.

The Swedish scientist Erik M. P. Widmark (1889–1945) made pioneering contributions to the knowledge about the pharmacokinetics of ethanol during the early decades of the twentieth century. Widmark observed that after the peak concentration in blood had been reached, the disappearance phase seemed to follow a near straight-line course, suggesting that the system for metabolizing alcohol was saturated (fully occupied), so that the amount of alcohol metabolized each hour did not depend on the amount in the blood. This situation is termed a *zero-order elimination process.* (Zero-order kinetics is contrasted with first-order kinetics, in which the metabolic system [e.g., the liver] is not saturated and in which the amount of drug metabolized per hour increases as the amount presented to the metabolic system increases.) Figure 1 (left frame) depicts zero-order elimination kinetics of ethanol after rapid intravenous infusion. Similar kinetics apply to the administration of alcohol, so, for example, if an individual drinks twelve standard drinks between 10 p.m. and 1 a.m., he or she will still have a detectable blood alcohol concentration at 7 a.m. Zero-order kinetics means that the rate of metabolism is at the maximal capacity and has a constant rate of approximately 7 to 10 grams per hour (equivalent to about one standard drink per hour) regardless of how much alcohol is consumed (Swift, 2003).

Zero-order kinetics implies that the elimination rate of ethanol is independent of the blood alcohol concentration (BAC) and, therefore, k_β should be the same regardless of the dose of ethanol administered; however, subsequent studies have shown that the slope of the BAC decay phase is steeper after larger doses of ethanol are ingested. Furthermore, when the BAC declines below about 10 mg/dl (0.01 g%, 2.17 mmol/l) the elimination curve

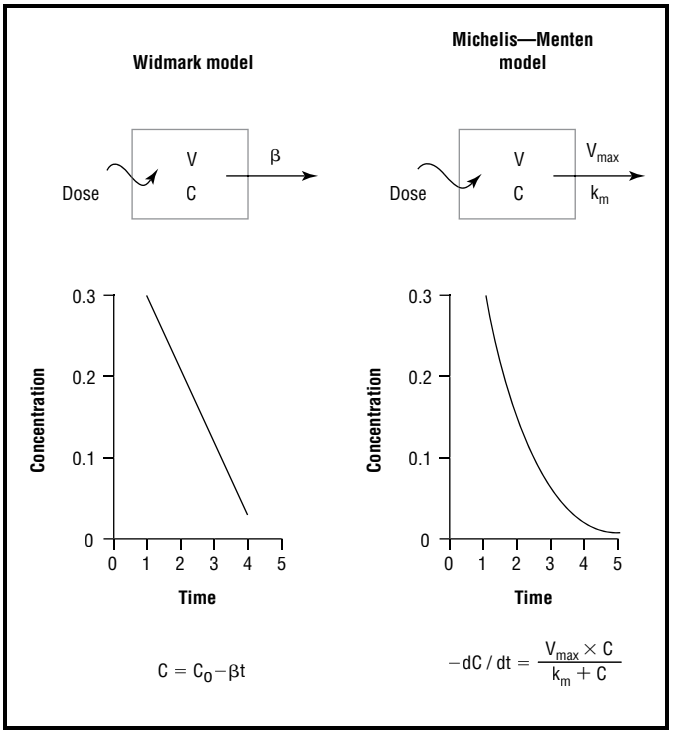

Figure 1. Schematic diagram illustrating the elimination kinetics of ethanol. The left frame shows Widmark's zero-order model. The right frame shows Michaelis–Menten (MM) capacity–limited kinetics. An intravenous bolus dose of ethanol enters a volume V to produce a concentration C; β is the zero-order elimination rate constant; V_{max} is the maximum velocity of the reaction; and k_m *is the Michaelis constant—the concentration of ethanol at half maximum velocity. Concentration-time profiles are shown for zero-order and MM kinetics, and the mathematical expressions for the elimination rates are given.* ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

of ethanol from blood flattens out and changes into a curvilinear decay profile.

Two different methods are described in the literature to portray the pharmacokinetics of ethanol. The method of choice seems to depend on the professional interests, the scientific background, and the training of those concerned. Specialists in forensic medicine and toxicology, as well as other disciplines, favor the mathematical approach developed by Widmark. In contrast, scientists with their basic training in pharmacy and pharmacology prefer Michaelis-Menten (MM) kinetics, that is, saturable or capacity-limited enzyme kinetics. The MM model is depicted in Figure 1 (right frame) after intravenous input of ethanol. A pseudolinear phase is evident for most of the elimination profile, provided that the BAC remains sufficiently high (> 10 mg/dl). At low substrate concentrations (C), a hockey-stick shape develops when data are plotted on cartesian graph paper. Accordingly, when C is much greater than k_m, the elimination rate approaches its maximum velocity; $-dC/dt = V_{max}$ (Figure 1, right frame). When C is less than k_m the elimination rate is proportional to the substrate concentration; $-dC/dt = (V_{max}/k_m)\ C$ and the MM equation collapses into first-order kinetics. This collapsing of the model is a consequence of capacity-limited kinetics and does not reflect any sudden change in the order of the biochemical reaction.

ETHANOL AS A DRUG

Ethanol differs from most other drugs in the way it is absorbed into the blood, metabolized in the liver, and how it enters the brain and produces its pharmacological effect. Ethanol (CH_3CH_2OH) has a molecular weight of 46.05, mixes with water in all proportions and carries only a weak charge; this means that the molecules of ethanol easily pass through biological membranes, including the blood-brain barrier. After absorption into the portal blood, ethanol passes through the liver, where enzymes begin the conversion into acetaldehyde and acetate. The end products of ethanol metabolism are carbon dioxide and water. The concentrations of ethanol in biological specimens depend on the dose ingested, the time after drinking, and the water content of the materials analyzed. The concentration-time profiles of ethanol and the pharmacokinetic parameters will differ depending on whether plasma, serum, urine, or saliva is the specimen analyzed. Several detailed reviews of ethanol pharmacokinetics are available and included in the bibliography.

Information about the absorption kinetics of ethanol is much less extensive than that about elimination kinetics. Unlike most other drugs, the dose of ethanol is not swallowed instantaneously because the drinking is usually spread over a period of time. For research purposes, however, ingestion of a bolus dose usually approximates drinking times of five to fifteen minutes. [The volume and concentration of ethanol, whether ingested as beer (3–6% w/v), wine (9–12% w/v), spirits (32–40% w/v), or as a cocktail (15–25% w/v), such that, for example, beer is less concentrated and consumed in greater volume than spirits, might influence the pharmacokinetic parameters. At lower alcohol concentrations, the portal blood concentration of alcohol is low, liver alcohol metabolizing enzymes are not saturated, and a higher proportion of alcohol is metabolized by the liver, leading to lower blood alcohol levels (Jones et al., 1997). Absorption of ethanol starts in the stomach where about 20 percent of the dose can become absorbed. The remainder is absorbed from the upper part of the small intestine. The speed of absorption of alcohol depends to a large extent on the rate of gastric emptying, which varies widely among different subjects. Because food in the stomach delays gastric emptying, food slows the rate of alcohol delivery to the intestine and the resulting peak blood alcohol level is lower. Food in the stomach acts this way by lowering the concentration of alcohol by dilution. This effect is more evident for small volumes of concentrated alcohol (spirits) than for larger volumes of more dilute alcohol (beer) (Roine et al., 1993). Assuming that the rate of absorption from the gut is a first-order process, one can represent the entire concentration-time profile of ethanol with a single equation: $C = C_o(1 - e^{-kt}) - k_\beta t$, where C = BAC at some time t after administration, C_o = initial BAC extrapolated BAC (see Figure 2), k = first-order absorption rate constant, k_β = zero-order elimination rate constant, and t = time after drinking. The peak BAC and the time of reaching the peak after drinking are important

Dose		Peak BAC mg/dl		k_0 mg/dl h		Time to peak (min)[3]			
g/kg[1]	N	mean	(range)	mean	(range)[2]	10	40	70	100
0.34	6	56	(43–67)	12	(9–14)	5	1	—	—
0.51	16	74	(54–91)	13	(10–14)	11	3	1	1
0.68	83	92	(52–136)	13	(9–17)	33	26	21	3
0.85	44	120	(83–178)	15	(12–18)	13	24	7	—

Maximum concentration of ethanol in capillary (fingertip) blood and the time of reaching the peak after end of drinking. The zero-order rate of elimination of ethanol from blood (k_0) is also given. The subjects drank neat whiskey within 15–25 minutes after an overnight 10-hour fast.
[1]g ethanol/kg = 0.036 oz ethanol/kg.
[2]Zero-order elimination rate.
[3]Number of subjects reaching their peak BAC at 10, 40, 70 and 100 min., measured from end of drinking.

Table 1. Peak blood alcohol concentration and time needed to reach the peak after end of drinking. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

aspects of the absorption kinetics. Table 1 gives examples of these parameters after healthy men drank undiluted whiskey (40% v/v or 80 proof) on an empty stomach. The absorption of ethanol occurs more slowly from the stomach than from the intestine owing to the enormous difference in the absorption surface available. The absorption of ethanol occurs progressively during a drinking binge or spree, and studies have shown that the BAC fifteen minutes after the last drink has reached about 80 percent of the final peak BAC. Because of the saturation-type kinetics, the peak BAC and the area under the curve (AUC) increase more than expected from proportional increases in the dose. The rate of delivery of ethanol to the liver determines the AUC for a given dose and vice versa. The systemic availability (bioavailability) of drugs such as ethanol with dose-dependent kinetics should not be calculated from the ratio of AUC after oral and intravenous administration.

THE WIDMARK EQUATION

Figure 2 gives examples of the concentration-time profiles of ethanol obtained from oral and intravenous administration of a moderate dose. The ratio of the dose administered (D) to the initial extrapolated concentration of ethanol in blood (C_o) is the apparent volume of distribution (V_d) having dimensions L/kg. This defines the relationship between the concentration of ethanol spread over the body weight (in kilograms, kg) and the concentration in the blood. $C_o = D/(kg \times V_d)$; $D = C_o \times kg \times V_d$ is known as the *Widmark equation*; it is widely used to estimate alcohol in the body from measurements of alcohol in the blood. Widmark found that the average V_d for men was 0.68, with a range from 0.51–0.85, but in women the volume of distribution was less—with an average of 0.55 and a range of 0.44 to 0.66. These differences between the sexes stem from differences in body-tissue composition; proportionally, women carry more fat but less water than do men. Accordingly, women reach higher BACs than men if the same dose of ethanol is given according to body weight. A similar observation was made in studies of men with widely different ages because body water decreases in the elderly. By dividing the dose of ethanol administered (g/kg) by the time needed to reach zero BAC ($time_0$) one obtains an estimate of the rate of clearance of ethanol from the body. This calculation neglects the nonlinear phase of ethanol elimination beginning at BAC below 10 mg/dl but does include the contribution from any first-pass metabolism occurring in the liver and gut.

A second equation, $D = kg \times V_d \times (C + k_\beta t)$ can be used to estimate the amount (dose D) of alcohol a person has consumed from knowledge of his or her BAC (C). Similarly, a third equation, $C = D/(kg \times V_d) - (k_\beta t)$ allows estimating the BAC (C) that might exist after drinking a known amount of ethanol. For best results when using these equations, absorption and distribution of ethanol must be complete at the time of sampling blood. Owing to inter- and intra-individual variations in the pharmacokinetic parameters V_d and k_β the results obtained are subject to considerable uncertainty. This uncertainty should be allowed for when these calculations are made for legal purposes, for example, in trials concerned with driving under the

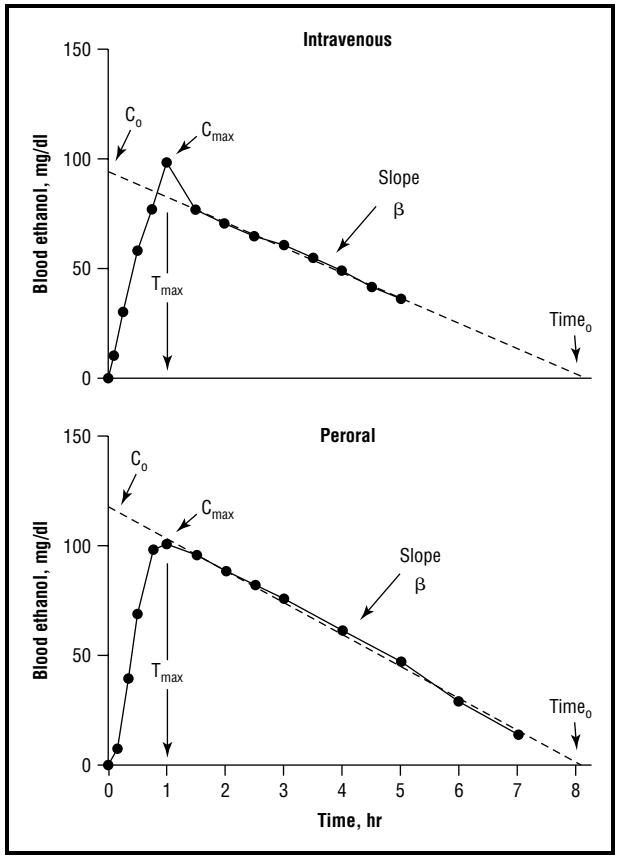

Figure 2. Examples of concentration-time profiles of alcohol taken by intravenous and oral routes of administration. Examples of concentration-time profiles of ethanol obtained after intravenous infusion of 0.4 g ethanol/kg body weight in 15 minutes (upper part) and after ingestion of 0.8 g/kg (lower part). Several key pharmacokinetic parameters are shown. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

influence of alcohol. A variability of ± 20 percent seems appropriate for most situations.

RESEARCH ON ADH

About 85 percent of the alcohol that enters the body is metabolized by hepatic enzymes responsible for ethanol oxidation (metabolism), but research has documented the existence of alcohol dehydrogenase (ADH)—the enzyme that transforms alcohol to acetaldehyde—in the gastrointestinal mucosa. Gastric ADH seems to be less effective in oxidizing ethanol in women (than in men) and in alcoholics (than in moderate drinkers). When a moderate dose of ethanol was ingested on an empty stomach, first-pass metabolism was negligible. This was explained by the ethanol bypassing gastric ADH, owing to rapid absorption occurring. However, the quantitative significance of gut metabolism in the overall disposal of ethanol remains controversial.

ELIMINATION RATES AND ENZYMES

Differences in the rate of disappearance of ethanol from blood might depend on genetic and environmental factors influencing the catalytic activity of an individual's alcohol-metabolizing enzymes. In humans, the enzyme ADH occurs in multiple molecular forms, designated class I, II, and III. Class I enzymes are located mainly in the liver cytosol and have a low km for ethanol. Various isoenzymes (enzyme variations within a class) exist and β_1-ADH (class I) is predominant in Caucasians, whereas β_1-ADH (class II) is the most abundant isoenzyme in Asians. The rate of ethanol elimination in the various racial groups is not much different from the variations seen within a single racial group in well-designed studies that allow for racial differences in body composition—the proportion of fat-to-lean body mass.

Alcoholics have a greater capacity to eliminate ethanol than do moderate drinkers, though the tolerance seen in alcoholics is not fully explained on this basis. The liver microsomes contain enzymes capable of oxidizing ethanol as well as other drugs, organic solvents, and environmental chemicals. One particular form of the cytochrome P_{450} enzyme (denoted P450IIEI) metabolizes ethanol. This microsomal ethanol oxidizing system (MEOS) has a k_m of 40–60 mg/dl (8.7–13 mmol/l) compared with 2 to 5 mg/dl (0.4–1 mmol/l) for human ADH. More importantly, the P450IIEI isoenzyme becomes more active during prolonged exposure to ethanol—a process known as enzyme induction. Accordingly, because of continuous heavy drinking, alcoholics develop a high capacity for eliminating ethanol from the blood. Their enhanced capacity vanishes after a short period of abstinence, however, but liver disease (hepatitis, cirrhosis) in alcoholics does not seem to impair their ability to dispose of ethanol.

BEHAVIORAL EFFECTS OF ALCOHOL

Studies have shown that the behavioral effects of ethanol and its associated impairment of performance are more pronounced when the BAC is rising than when it is falling. This observation seems to depend, at least in part, on the distribution of ethanol between blood and tissue. The arterial blood concentration of ethanol pumped to the brain exceeds the

concentration measured in the venous blood, which is returning to the heart from skeletal muscles. This arterial-venous difference is most pronounced shortly after drinking; it decreases as ethanol diffuses equally into all body fluids. It seems that this is not the whole story because some evidence points to the development of acute cellular tolerance to ethanol's effects—an aspect of tolerance that develops quickly.

Despite extensive studies of ethanol pharmacokinetics spanning many years, there are still a number of unsettled issues and areas of debate. Two such issues are (1) the practical advantages of Michaelis-Menten kinetics as opposed to Widmark's zero-order model and (2) the role of gastric ADH in the presystemic extraction of ethanol.

See also **Pharmacokinetics: Implications for Abusable Substances.**

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PHARMACOLOGY. In its broadest sense, pharmacology can be defined as the science dealing with interactions between living systems and molecules—in particular, chemicals (i.e., drugs)—usually introduced from outside the system. This definition also includes medical pharmacology, which is the science of drugs used to prevent, diagnose, and treat disease. Also included are the important roles played by chemicals in the environment that can cause disease, as well as the use of certain chemicals as molecular probes for the study of normal biochemistry and physiology. Toxicology is the branch of pharmacology that deals with the undesirable (i.e., toxic) effects of chemicals in biological systems.

See also **Drug; Drug Metabolism; Drug Types; Pharmacodynamics; Pharmacokinetics: General; Poison.**

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PHENCYCLIDINE (PCP). Phencyclidine is a recreational drug. Although phencyclidine (PCP) and drugs of similar chemical structure (arylcyclohexylamines) are often called hallucinogens, they rarely produce hallucinations, and the sensory distortions or apparent hallucinations that are produced are not the same type as LSD-induced hallucinations. Instead, phencyclidine belongs to a unique class of drugs called the dissociative anesthetics. Phencyclidine was developed in the 1950s as an anesthetic for veterinary medicine and later was tested in human surgical patients. There was great potential for PCP as an anesthetic because it produced minimal effects on the heart and did not suppress breathing. Unfortunately, the adverse side effects of PCP (e.g., dysphoria [unhappy, ill] and psychotic symptoms) led to a termination of the human clinical trials. The drug is no longer manufactured for veterinary use because supplies were stolen and the drug became widely abused in the 1970s. Ketamine, a drug chemically similar to PCP, is now used as a veterinary anesthetic and in special cases for anesthesia in humans. This drug is less powerful and shorter-acting than PCP.

Phencyclidine abuse, mainly in pill form, peaked in the late 1970s and markedly declined throughout the 1980s and 1990s. The most common route of administration in use in the 2000s was smoking. Phencyclidine is often added to marijuana cigarettes, and it is commonly used while people are also drinking alcoholic beverages. Street names for PCP are "angel dust" or "crystal"; it is called "space base" when combined with cocaine.

MECHANISM OF ACTION

Most investigators agree that the behavioral effects of PCP are mediated predominantly through receptors, which are proteins that are important for the normal functioning of cells within the body. Phencyclidine acts as an antagonist at the N-methyl-D-aspartate (NMDA) receptor-channel complex, which is one type of excitatory amino acid receptor that is selectively activated by the agonists NMDA and glutamate. By definition, agonists produce stimulation while antagonists block the effects of agonists. When either glutamate or NMDA bind to the receptor, a channel within the cell membrane, opens to allow sodium, calcium, and potassium ions to flow into and out of the cell. This movement of ions across the cell membrane causes a depolarization of the membrane, which, if sufficiently large, causes the cell to fire. When the cell fires, an electrical charge passes along its membrane and neurotransmitters (chemicals that allow cells to communicate with each other) are released. Thus, glutamate and NMDA are important for normal cell-to-cell communication within the body.

PCP, as well as TCP, ketamine, dizocilpine (MK-801), and SKF 10,047, is representative of compounds that act as noncompetitive antagonists at the NMDA-receptor complex. The binding site for PCP resides within the channel. Binding to this site physically prevents calcium and sodium ions from entering the cell while at the same time preventing potassium ions from leaving the cell. Blocking the movement of ions through the cell membrane in turn prevents the neuron from firing. In contrast to the noncompetitive antagonists, competitive antagonists such as CGS 19755, NPC 12626, CPP, and AP5 bind to the NMDA receptor itself without causing the ion channel to open. By simply occupying the receptor without activating it, competitive antagonists prevent NMDA from binding to and activating the receptor. Unlike noncompetitive antagonists, competitive NMDA-antagonist effects can be surmounted by higher doses of the agonist. However, the end result of both noncompetitive and competitive antagonists is a reduction of neuronal firing.

PHARMACOKINETICS AND METABOLISM

PCP use in humans occurs through several routes of administration, including intranasal (snorted), intravenous, oral, and inhalation (smoked). When PCP is smoked in parsley cigarettes, approximately 70 percent of the total amount of PCP is inhaled. Of this amount, 38 percent is inhaled as PCP and 30 percent is inhaled as phenylcyclohexene, a by-product of PCP created when it is heated. Peak blood concentration of PCP occurs after only five to ten minutes, which is occasionally followed by a second peak one to three hours later. PCP is predominantly excreted in urine after intranasal, intravenous, and oral administration. The rate of PCP elimination through the kidneys depends on both urine pH and urine-flow rate. More specifically, PCP elimination occurs more rapidly when urine is acidic and when urine is passed rapidly.

DISCRIMINATIVE STIMULUS EFFECTS

One useful method of evaluating the pharmacological characteristics of PCP, as well as a variety of other drugs, is the drug-discrimination procedure. Typically, animals that are slightly food-restricted are trained to respond for food on one lever after drug administration and on another lever after saline. On days when the drug is administered before the session, responding on the drug-associated lever results in food delivery while responding on the saline-associated lever does not. Conversely, on days when saline is administered before the session, responding on the saline-associated lever results in food delivery while responding on the drug-associated lever does not. After a number of training days, animals learn to reliably respond on the drug lever after the drug injection and on the saline lever after saline injection. Once this discrimination has been established, a number of test drugs can be administered to determine whether or not they produce effects similar to the training drug. Test drugs that substitute for the training drug (i.e., cause responses on the drug-associated lever) are assumed to have discriminative stimulus effects that are similar to the training drug.

Using this procedure, several investigators have shown that PCP and other noncompetitive antagonists produce similar discriminative stimulus effects in a number of different species (see Willetts, Balster, & Leander, 1990 for a review). These results suggest that the mechanisms of action of PCP and such other noncompetitive antagonists as ketamine and dizocilpine, are similar. Furthermore, the discriminative stimulus effects of competitive antagonists such as CGS 19755, NPC 12626 and CPP were also similar to each other, which is again consistent with the notion that the mechanisms of action of competitive antagonists are similar. Given that competitive and noncompetitive antagonists both reduce neuronal firing, it was of interest to compare the discriminative stimulus effects of these two types of antagonists. In most species, the discriminative stimulus effects of competitive and noncompetitive antagonists are very different from each other.

Another difference between the competitive and noncompetitive antagonists lies in their abilities to antagonize the discriminative stimulus effects of NMDA. While both types of antagonist are effective in blocking the convulsant and lethal effects of NMDA, competitive antagonists in general are much more effective than noncompetitive antagonists in blocking the discriminative stimulus effects of NMDA. The noncompetitive antagonists partially antagonize NMDA but only at doses that produced substantial behavioral suppression. While most effects of NMDA are antagonized by both competitive and noncompetitive antagonists, the behavioral-suppressing effects of noncompetitive antagonists often interfere with their ability to antagonize the discriminative stimulus effects of NMDA.

Finally, another important finding with competitive and noncompetitive antagonists involve their interaction with other receptor systems. Studies show that the discriminative stimulus effects of competitive antagonists such as CPP and NPA 12626 are similar to those produced by the barbiturate pentobarbital. Under certain conditions, the discriminative stimulus effects of PCP and pentobarbital were also similar. In addition to the interactions of NMDA antagonists with barbiturate receptors, some investigators have found similarities between PCP and ethanol (alcohol). These studies have proven to be important in describing both the similarities and differences between the noncompetitive and competitive NMDA-receptor antagonists.

TOLERANCE

Tolerance to a drug occurs when increasingly higher doses are needed to produce a specific effect or if drug effects diminish after repeated administration of the same dose of the drug. It has not been possible to study tolerance to PCP in human subjects; but when interviewed, PCP users report that they increase the amount of PCP that they take over time (Carroll, 1990). Another indicator of tolerance development is that burn patients treated with ketamine for pain often require higher doses over time. It is easier to study tolerance to ketamine, PCP, and similar drugs in animals. Laboratory studies with rats have shown that tolerance developed to the effects of PCP on food-reinforced responding; to the effects of PCP and dizocilpine on steroid hormone (adrenocorticotropin and corticosterone) release; and to the cataleptic effects of ketamine. Supersensitivity, the opposite of tolerance, occurs when repeated drug exposure produces a greater effect at a given dose. Some investigators have found that tolerance develops to some effects of PCP, such as head weaving, turning, and backpedaling, while supersensitivity occurs with such other behaviors as sniffing, rearing, and ambulation. Although some scientists have hypothesized that PCP tolerance and supersensitivity are mediated through non-NMDA-receptor systems, others have suggested that PCP tolerance may be mediated through the NMDA receptor system. Repeated administration of dizocilpine, a PCP-like compound, produced a reduction in the number of NMDA receptors in the rat brain, and that was correlated with tolerance to some of the behavioral effects produced by dizocilpine. Further studies will clarify the role of different receptor systems in the development of tolerance to the effects of PCP and related compounds.

Studies indicate that there are interactions between PCP and other drugs with respect to tolerance and supersensitivity of drug effects. For example, dizocilpine blocked the development of tolerance to morphine's analgesic (painkilling) effects, but it did not alter the analgesic effects when morphine was administered acutely. Also, dizocilpine attenuated the development of tolerance to ethanol (alcohol), and it inhibited sensitization to amphetamine and cocaine (*DHHS Fourth*

Triennial Report to Congress on Drug Abuse and Drug Abuse Research, 1992).

DEPENDENCE

Physiological dependence on a drug is usually defined by a set of withdrawal symptoms that occur when steady use of the drug is discontinued. The withdrawal symptoms are typically the same for a given drug, and they follow a specific time course that ranges from about six to forty-eight hours, depending on the drug. The withdrawal symptoms may be rapidly reversed after one administration of the drug.

Most of what is known about PCP dependence is from experimental studies with animals. There are only limited reports of PCP withdrawal effects in humans. In 1981, Tennant and colleagues studied sixty-eight regular PCP users; they found that one-third of them had sought treatment or medication to relieve the effects of PCP withdrawal. Withdrawal symptoms that they commonly reported were depression, drug craving, increased appetite, and increased need for sleep. Another way PCP dependence has been documented in humans is in studies of babies born to PCP-using mothers. Withdrawal signs that have been noted are diarrhea, poor feeding, irritability, jerky movements, high-pitched cry, and inability to follow a stimulus visually.

In laboratory studies with monkeys, similar signs of PCP withdrawal have been noted. Balster and Woolverton (1980) gave rhesus monkeys continuous access to PCP directly into the blood stream for fifty days, using an intravenous cannula system. The monkeys were trained to respond on a lever for an infusion of PCP. When PCP was replaced with a salt and water solution used to dissolve the drug (vehicle), withdrawal signs were noted, such as poor feeding, weight loss, irritability, bruxism (grinding of the teeth), vocalizations, piloerection (hair standing up), tremors, less exploratory behavior in the cage, and poor motor coordination. The withdrawal syndrome began within four to eight hours, peaked between twelve and sixteen hours, and had disappeared by twenty-four to forty-eight hours. These results have been repeated in studies with rats. Some studies have reported PCP withdrawal effects after as little as two weeks of exposure. Thus long-term use of the drug may not be necessary to produce physical dependence.

Recent studies with animals have shown that not only a short period of exposure to PCP but low doses of PCP result in withdrawal effects when drug administration is discontinued. Operant conditioning experiments are used as sensitive tests of drug-withdrawal effects in animals. In these experiments, animals are trained to respond on a lever or push a button or other device to obtain a food reward. At the same time they are allowed to self-administer drugs orally or intravenously. When drug access is removed, a decrease in operant response to food is often seen, even when the drug dose is sufficiently low to produce no observable signs of withdrawal. These measures have also been used to demonstrate withdrawal effects from such drugs as cocaine, caffeine, and nicotine. When regular use of these drugs is discontinued there are no observable signs of withdrawal during abstinence. The most severe reductions in the operant behavioral baselines occur during the first forty-eight hours of drug withdrawal, a time during which physical signs occur when higher maintenance doses are used; however, the behavioral disruptions often last for long periods of time. During withdrawal, when animals will not respond on a lever for food, they readily consume hand-fed food. Thus, the decrease in feeding may not be due to illness but to a decrease in the motivation to work for food.

In the first study that demonstrated disruption in operant behavior during PCP withdrawal, Slifer and coworkers (1984) treated monkeys with continuous intravenous infusions for ten days. They were required to make 100 responses on a lever for each food pellet. When access to PCP was terminated, responding for food decreased substantially for up to seven days and did not return to normal levels until the monkeys were again allowed access to PCP. Similar results were found by other investigators using monkeys trained to self-administer orally delivered PCP. There was little difference in the results, depending on whether the PCP was self-administered or experimenter-administered. In the monkey studies, there was only a weak relationship between dose and the severity of the withdrawal effect; but in rats, PCP dose, blood levels, and magnitude of the withdrawal effect were closely related. Recent studies have shown that there is cross-dependence between drugs

that are chemically similar to PCP—such as PCP and ketamine, dizocilpine, and the (+)isomer of SKF-10,047; however, cross-dependence was not demonstrated with either the racemate or (−)isomer of SKF-10,047 or with ethanol.

The PCP-withdrawal effect can be altered by changing schedules of reinforcement. In one study with monkeys, lever-press requirements or fixed ratios (FRs) for food were increased from 64 to 128 to 256 to 512 to 1024, and PCP-withdrawal effects were examined at each value. As the FR value increased, PCP withdrawal effects became more pronounced. At the two higher FRs, body weights declined and the severity of the withdrawal effect showed no further increases. To examine the effects of amount of food available, another experiment was conducted in which the FR was held constant at 1024 and the monkeys were either supplemented with 100 grams of hand-fed food or not. The amount of responding for earned food remained the same during supplemented and unsupplemented conditions, but when the effects of withdrawal were examined, a disruption in responding occurred only under the supplemented condition. When the monkeys had to earn their entire daily food ration, the withdrawal effect disappeared. These studies suggest that the severity of the PCP withdrawal effect is determined by the behavioral economics of food availability. The magnitude of PCP withdrawal increased as the price (FR of food) increased; but as the price became so high that body weight was lost, the PCP-withdrawal effect entirely disappeared. These data also suggest that PCP withdrawal is not necessarily an illness but a decreased level of motivation.

The use of drugs to treat the PCP-withdrawal syndrome has produced mixed results. When monkeys had access to orally delivered (+)SKF-10,047, the PCP-withdrawal-induced disruptions in food-maintained responding were reversed. This was not the case with (−)SKF-10,047 or the racemate (±)SKF-10,047. Injections of dizocilpine before PCP withdrawal, or two days into PCP withdrawal, greatly reduced or reversed, respectively, the disruptions in food-reinforced responding. Dizocilpine also dose-dependently reduced PCP self-administration. In contrast, while buprenorphine, a partial agonist at the mu-opiate receptor, also dose-dependently reduced PCP self-administration, it had no effect on PCP-withdrawal-induced disruptions in food-maintained responding. When PCP was self-administered concurrently with ethyl alcohol (ethanol) and then PCP access was removed, PCP-withdrawal effects were as severe as when ethanol had not been available. Thus ethanol did not alleviate the PCP withdrawal effect; although, as noted earlier, PCP and ethanol share discriminative stimulus effects (Grant et al., 1991). In other studies, PCP was self-administered concurrently with ethanol or caffeine. When PCP and the other drug were removed simultaneously, the withdrawal disruption was more severe than when PCP alone was withdrawn. (Further details of these withdrawal studies may be found in reviews by Carroll [1990] and by Carroll and Comer in the *DHHS Fourth Triennial Report to Congress on Drug Abuse and Drug Abuse Research*, 1992.)

REINFORCING EFFECTS

The reinforcing effects of a drug are determined by demonstrating that self-administration of the drug plus the solution it is dissolved in (vehicle) occurs in excess of self-administration of the vehicle alone. When drug-reinforced behavior is readily achieved in the animal laboratory, it is usually a good predictor that the drug has considerable abuse liability in the human population. The reinforcing effects of PCP have been studied using two animal models of self-administration, oral and intravenous. The intravenous route of self-administration requires the animal to make a specified number of responses on a lever or other manipulandum within a predefined time—then a fixed dose of the drug is delivered by an infusion pump via a catheter that is surgically implanted in a large vein that leads to the heart. Studies from various laboratories have demonstrated that intravenously delivered PCP functions as a reinforcer for rats, dogs, monkeys, and baboons.

Drugs that are chemically similar to PCP are also self-administered intravenously. These include drugs that have similar receptor-binding sites in the brain, such as ketamine, (+)SKF-10,047, dexoxadrol, and cyclazocine; and phencyclidinelike drugs that function as noncompetitive antagonists at the NMDA receptor, such as dizocilpine. Phencyclidine and dizocilpine self-administration is more reliably obtained when the animal has a history of self-administration of a drug with similar pharmacological or discriminative-stimulus effects. It has also been found that drugs that share

discriminative-stimulus effect with PCP, such as (+)SKF-10,047, ketamine, PCE, TCP, and ethanol, are readily substituted for PCP in self-administration studies.

Oral PCP self-administration is established by presenting gradually increasing concentrations of PCP after the animal is given its daily food ration. After sufficient quantities of PCP are consumed, food is given after the drug self-administration session, and PCP consumption usually persists. This procedure provides a long-term stable baseline to examine variables that affect PCP-reinforced behavior. For example, alternative nondrug reinforcers, such as saccharin, reduce PCP-reinforced responding up to 90 percent of baseline if the FR for PCP is high or if the PCP concentration is very low. Free access to food decreases PCP self-administration, while even small reductions in the daily food allotment markedly increase PCP self-administration. Concurrent availability of ethanol also reduces PCP-reinforced responding.

A limited amount of information is available concerning drug pretreatment and PCP self-administration. Buprenorphine and dizocilpine pretreatment both resulted in dose-dependent decreases in PCP self-administration; however, potential treatment drugs such as fluoxetine and carbamazepine had no effect. Treatment with other drugs such as amphetamine or pentobarbital had a biphasic effect on PCP self-administration. Low doses of the pretreatment drugs increased PCP self-administration and high doses decreased PCP self-administration.

TOXICITY

There is little evidence that long-term PCP use in adult humans (Luisada, 1981) and monkeys (see *DHHS Fourth Triennial Report to Congress on Drug Abuse and Drug Abuse Research*, 1992) results in any detectable organ or cellular damage. In monkeys that had been self-administrating PCP for eight years, tests of all organ systems, clinical chemistries, physical exams, and X rays revealed no differences between PCP-experienced and control animals that were the same age but had little drug experience. In humans, the form of toxicity most commonly associated with PCP use is a change in behavior. There have been a few accounts of bizarre and/or violent behavior associated with PCP use. Such reports have diminished since the preferred route of self-administration has shifted from oral (pill) to inhalation, which offers the users an ability to more carefully control the dose.

In monkeys, PCP produces a calming, tranquilizing effect. The immediate effects in humans are not seen in the hospital or clinic. Instead, the PCP user arrives in the emergency room several hours after PCP use, possibly while suffering acute withdrawal effects. Approximately twelve to fifteen hours after PCP was last taken, monkeys become agitated, violent, and aggressive. It is possible that many of the early reports of human violence and PCP-related homicides were related to the withdrawal effects. It is necessary to determine the time course of unusual behavior and important to know the time of drug intake, although this is difficult to establish because the patient often loses memory of the drug-taking event.

Another unusual aspect of PCP toxicity is that users often complain of unpleasant effects long after chronic use has stopped. These reports could be caused by the fact that PCP is highly fat-soluble and becomes stored for long periods of time in body fat. During periods of weight loss, there is subsequent mobilization of fat-stored PCP into blood and brain tissues. Recent laboratory research with rats supports this hypothesis by demonstrating the ability of food deprivation to increase PCP levels in blood and brain (Coveney & Sparber, 1990).

Increasing data have become available on the effect of drugs of abuse on the offspring of dependent mothers, and it appears that the offspring of PCP users may be more vulnerable to the adverse effects of PCP than their adult counterparts. Golden and coworkers (1987) studied ninety-four PCP-exposed newborns and ninety-four nonexposed controls; they found neurological abnormalities such as abnormal muscle tone and depressed reflexes in the exposed group. Another study followed twelve exposed infants for eighteen months and found a high percentage of medical problems (Howard et al., 1986). At six months the infants were irritable and hyperresponsive, and later they showed varying degrees of abnormalities in fine motor, adaptive, language and social skills. A recent study of the offspring of forty-seven PCP abusers and thirty-eight nonusers found that neurological dysfunction was common in the

infants of PCP-abusing mothers (Howard, Beckwith, & Rodning, 1990). There was greater apathy, irritability, jitters, and abnormal muscle tone and reflexes. Follow-up interviews at six and fifteen months, using the Gesell Developmental Exam, revealed poor language development and a lower developmental quotient in general; however, the long-term outcome for PCP-exposed newborns is unknown.

TREATMENT

There are currently no PCP antagonists that are useful for treatment of PCP overdose. Symptomatic treatment may be given for suppressed breathing rates, fever, high blood pressure, and increased salivation. Convulsions are treated with diazepam. Elimination of the drug may be enhanced by making the urine more acidic and/or pumping stomach contents. Attempts to minimize environmental stimuli have helped to control violent and self-destructive behavior. Psychiatric care may be needed for an extensive psychotic phase that may follow overdose (Jaffe, 1989).

See also **Abuse Liability of Therapeutic Drugs: Testing in Animals; Addiction: Concepts and Definitions; Aggression and Drugs: Research Issues; Fetus, Effects of Drugs on the; Phencyclidine (PCP): Adverse Effects; Research, Animal Model: An Overview; Research: Drugs as Discriminative Stimuli; Tolerance and Physical Dependence.**

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PHENCYCLIDINE (PCP): ADVERSE EFFECTS.

Widely known as PCP, phencyclidine is an important drug of abuse in the United States, even though its use has declined since the 1980s. PCP is difficult to classify pharmacologically and is considered separately from the hallucinogens. The drug has not been studied systematically in animals, although research done in 1973 and 1980 indicated that it produces dependence in monkeys. Its effects on the human central nervous system are generally unpleasant. It produces a unique type of hallucinatory effect and is used both by smoking and ingestion. Persons under the influence of PCP experience mood changes, perceptual distortions, and feelings of dissociation from their surroundings. Since their judgment is impaired, they may take unnecessary risks. They may become unpredictable and violent. In certain individuals, PCP use, especially if repeated often, can result in the production of a mental disturbance referred to as PCP psychosis. It is not, however, known with certainty whether PCP itself, or a combination of factors involved in the lifestyle of PCP abusers, is the cause of brain damage or of long-term behavior impairment that also sometimes occurs in PCP abusers.

HISTORY

Phencyclidine was developed in the 1950s for use as an anesthetic, but its use was discontinued because patients developed delusions, severe anxiety, or frank psychosis after their operation. It was also used by veterinarians as an anesthetic for some years; at present, however, all PCP sold on the street is manufactured illegally. The initials "PCP" are derived from a nickname, "The Peace Pill." The history of PCP as a drug of abuse began in the United States in the mid-1960s, when it was primarily taken by ingestion; but the real epidemic of PCP abuse occurred in the 1970s, when smoking and insufflation ("snorting") became the more common forms of use (Burns & Lerner, 1976). Because it is not difficult for an experienced chemist to synthesize the drug, PCP and its abuse spread rapidly, peaking about 1978. After 1980, its prevalence declined—however, PCP abuse continues to occur precisely because the drug is relatively easy to make. National Institute on Drug Abuse surveys show that PCP abuse remains a significant public health problem. PCP abuse remains a significant public health problem. As of 2008, most PCP abusers either snort PCP powder, ingest PCP pills, or smoke it by sprinkling it on smoking material (mint leaves, parsley, marijuana, or tobacco). Users also dip cigarettes in liquid PCP and smoke them.

PSYCHOLOGICAL EFFECTS OF PCP

The psychological effects of PCP abuse can be discussed under three headings: (1) effects accompanying acute intoxication, (2) personality disturbances that can sometimes develop in PCP abusers, especially when associated with chronic use, and (3) possible neurobehavioral toxicity that may result from chronic use.

SIGNS AND SYMPTOMS OF PCP INTOXICATION

Low Dose. Dreamy carefree state, mood elevation, heightened or altered perception, impaired judgment, partial amnesia.

Intermediate Dose. Inebriation, motor incoordination, dissociation and depersonalization, confusion and disorientation, perceptual distortions and preoccupation with abnormal body sensations, diminished pain sensitivity, partial amnesia, and sometimes exaggerated mood swings and panic.

High Dose. Catatonia, "blank stare," drooling, nystagmus (eye-rolling), delirium and hallucinations, psychotic behavior, severe motor incoordination, total amnesia.

ACUTE PCP INTOXICATION

As with all drugs, the effects of PCP depend on the dose that is taken. The section above lists the typical effects of PCP at various doses. PCP abusers usually adjust their dosage to experience only the low-dose effects. High-dose effects are similar to a mild type of dissociative anesthesia.

Experienced drug abusers can readily distinguish the experience of PCP intoxication from that produced by other drugs such as marijuana, mescaline, and lysergic acid diethylamide (LSD). Users typically report a feeling of dissociation from the environment and abnormal body sensations and body image. The perceptual distortions often cause objects to appear far away or abnormal in size. Compared to LSD, the effects of PCP are not very psychedelic.

The most dangerous effects of PCP intoxication arise from the impaired judgment and altered perceptions that occur. People can engage in risk-taking behavior and harm themselves or others. Driving, swimming, or other activities requiring coordination and good judgment become extremely dangerous. Someone on PCP may also engage in casual but high-risk sexual behaviors. PCP users experience profound mood swings—in which what begins as a pleasant experience can turn into panic and terror—and their behavior is unpredictable. Sometimes these "bad trips" can lead to violent and uncharacteristic behaviors with disastrous results. In cases of high-dose intoxication, users can experience a toxic psychotic episode with delirium, profound hallucinations, and paranoia. In cases of severe overdose, seizures, stroke, or kidney failure may lead to death (Burns & Lerner, 1976).

MEDICAL TREATMENT

As of 2008, there is no medication that can serve as an antagonist to the effects of PCP or that can speed up its excretion. PCP is easily soluble in fats, thus can remain in the central nervous system for long periods. A patient who has overdosed on PCP must be placed on life support. Patients with anxiety or seizures can be given diazepam (Valium). Patients with psychotic

episodes are usually treated with haloperidol (Haldol). Chlorpromazine (Thorazine) should *not* be given to patients who have taken PCP, as it may produce hypotension. Patients with severe hypertension due to PCP should be given diazoxide (Proglycem). Gastric lavage has been used successfully to treat patients who have ingested PCP directly.

PCP intoxication is considered a psychiatric emergency. It is recommended that these patients be placed in a secure room under observation. The health professional should not attempt to "talk the patient down." Physical restraints or a sedative such as lorazepam (Ativan) may be needed if the patient becomes violent.

LONG-TERM USE

In persons who abuse PCP in large amounts over a long period, or in those who have psychological problems that make them especially vulnerable, a chronic psychosis may develop. This PCP psychosis is evident even when abusers are not high on PCP, and it may be quite difficult to treat. The symptoms of PCP psychosis differ considerably from person to person; but patients may show many features of schizophrenia, including the appearance of a thought disorder, paranoid ideation, hallucinations, mood changes, and aberrant behavior. These patients often require psychiatric hospitalization and treatment with antipsychotic medications. In research studies in which PCP has been given repeatedly to animals, it has been possible to show the development of physical dependence (e.g., Balster & Woolverton, 1980). The doses required for dependence are quite high, so it may be that dependence in human PCP abusers is difficult to develop. There have been some clinical reports of withdrawal effects in heavy PCP abusers, but these do not appear to be present in most individuals needing treatment for PCP abuse. There are no specialized treatment methods for PCP abusers, and since many PCP abusers also abuse other drugs and/or alcohol, they are usually helped by the same counseling and psychotherapy programs that are used for other forms of drug abuse.

NEUROPSYCHOLOGICAL AFTEREFFECTS OF PCP ABUSE

It is not known for certain whether PCP causes brain damage or long-term neurological or behavioral impairment in chronic abusers. Although some PCP abusers develop neurobehavioral impairment, controlled experiments of the type that would need to be carried out to show that PCP alone was the cause of the problems have not been done. PCP abusers typically abuse many other drugs in addition to PCP, which may contribute to their problems, and they may have lifestyles and health habits that lead to neuropsychological dysfunction. For example, while under the influence of PCP, they may be involved in an accident resulting in brain injury, so the risk factors that accompany PCP abuse may be responsible for the clinical problems sometimes seen in abusers. It should be pointed out that PCP was used in humans for medical research for a number of years, and ketamine—a close analog of PCP—is, even in the early twenty-first century, given to thousands of patients, though only under close supervision. No legacy of neuropsychological impairment is seen in these individuals.

Does this mean that chronic PCP abuse does not cause neuropsychological impairment? Certainly, PCP—like all drugs—must be considered as a possible source of neural damage. In animal testing, it was found that even a single injection of a fairly high dose of PCP produced reversible pathomorphological changes in neurons of the cingulate and retrosplenial cortex in the brains of rats (Olney, Labruyere, & Price, 1989). Although it is not known if PCP produces these effects in humans, it is possible that it does and that this could lead to adverse health effects. Another possibly important basis for concern comes from studies which show that PCP, and related drugs, impair learning and memory in various animal models. PCP's ability to do this may be greater than for other classes of drugs of abuse, possibly due to PCP's ability to interfere with specific brain mechanisms for learning that involve N-methyl-D-aspartate (NMDA) receptors.

PCP AND VIOLENCE

Many people associate the abuse of PCP with violence and aggression, so this concern deserves special mention. Those under the influence of PCP often behave erratically and exercise poor judgment. These effects of PCP could certainly lead to violent behavior, and there are certainly numerous examples of extremely violent acts being performed by persons under the influence of PCP. This raises the question of whether PCP is uniquely associated

with the production of violence and aggression: Is someone intoxicated with PCP more likely to be violent than someone who is intoxicated with cocaine or alcohol?

Unfortunately, the answer to this question is not known. A great deal of criminal conduct in the United States is certainly carried out by people under the influence of alcohol or drugs. In addition, the public often associates drug use they do not understand with criminal and violent behavior. Every new drug epidemic is greeted with public concern that this drug causes violence. There is also the common practice of criminal attorneys using the defense of diminished capacity because of drug use to lessen the responsibility that their clients might bear for criminal conduct. All these factors undoubtedly contribute to the public attention focused on the relationship of PCP to violence.

Few good research studies have attempted to determine the specific role that PCP abuse may have in crime and violence. In one study (Wish, 1986) of nearly five thousand arrestees in New York City in 1984 who agreed to leave a urine specimen for drug analysis, it was found that 56 percent tested positive for at least one drug of abuse. For those who had used PCP recently, most had committed robbery, not bizarre violent offenses. In fact, assault was more common among arrestees who had not used PCP than among those who had. These results support the conclusion that PCP may be no more likely to cause violence than some other drugs of abuse—but clearly more research on this question is needed.

The National Institute on Drug Abuse estimates that as many as six million Americans have tried PCP at least once. The very large majority of these occasions of PCP use were not associated with violent acts; however, if some users prone to violence take PCP and are faced with a threatening situation, they may act unpredictably and violently. Although there is no scientific evidence that PCP actually increases muscular strength, PCP users unmindful of their own potential safety or injuries can be a formidable risk, so law enforcement personnel are on guard against these dangerous situations. Alternatively, it should not be assumed that most people who abuse PCP will become violent—nor should every inexplicable act of violence be casually or speculatively attributed to PCP abuse.

See also **Addiction: Concepts and Definitions; Amphetamine Epidemics, International; Complications: Mental Disorders; Crime and Drugs; Tolerance and Physical Dependence.**

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PHENOBARBITAL. This is the prototypic barbiturate central nervous system (CNS) depressant. It is prescribed and sold as Luminal and was introduced into clinical medicine in 1912. It was used for a long period as a sedative-hypnotic drug but has now largely been replaced by the much safer benzodiazepines.

Phenobarbital's long duration of action makes it useful for treating many forms of general and partial seizure disorders, such as epilepsy. Chronic use can result in tolerance and physical dependence, so it is classified as a Schedule III drug under the Controlled Substances Act. Chronic treatment with phenobarbital can increase the activity of certain liver enzymes that metabolize other drugs. Thus a potential side effect is that other drugs (e.g., steroids, oral anticoagulants, digitoxin, beta-blockers, oral contraceptives, phenytoin, and others) are metabolized more quickly—and their effectiveness is reduced. Combinations of phenobarbital and other CNS depressants, such as alcohol (ethanol), can lead to severe motor impairment and reduced breathing.

See also **Drug Interactions and Alcohol; Drug Metabolism.**

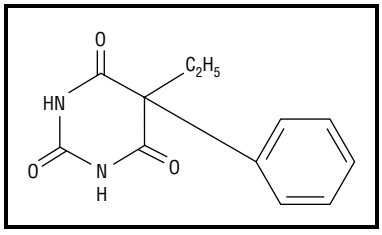

Figure 1. Chemical structure of phenobarbital. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

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SCOTT E. LUKAS

PHYSICAL DEPENDENCE. Physical dependence is a state produced by repeated or prolonged drug exposure in which the presence of the drug in the body is required to maintain normal physiological function. This state is recognizable only by the occurrence of a withdrawal reaction when the drug is removed, which is reversed when the drug is again administered. Such dependence is believed to result from adaptive changes in the nervous system, opposite in direction to the drug effects, which offset these effects when the drug is present and produce a drug-opposite effect in its absence. Physical dependence is not synonymous with addiction and can occur in nonaddicted persons.

See also **Addiction: Concepts and Definitions; Models of Alcoholism and Drug Abuse; Tolerance and Physical Dependence.**

HAROLD KALANT

PHYSICIANS AND MEDICAL WORKERS, SUBSTANCE ABUSE AMONG. Physicians and other health professionals (HPs) are not spared the ravages of addiction. In fact, some of history's most prominent physicians were addicted to drugs. Dr. William Halsted, known as the "Father of Modern Surgery," (innovator of blood transfusions, intravenous fluid therapy, and gall bladder surgery) was addicted to cocaine, while practicing, in the late 1800s. His friend, Sir William Osler, another prominent physician at Johns Hopkins University, attempted to wean Halsted off cocaine by using morphine.

Until the early twentieth century, medical practice went largely unregulated. As state medical regulatory boards evolved, their role was to assure that

physicians received legitimate education and degrees. Not until the mid-1900s did medical boards begin to protect the public from impaired physicians.

Addicted HPs are excellent subjects to study because they are usually accessible both prior to and after treatment, and money is not a limiting factor in their receiving good treatment. The more than thirty types of licensed HPs include physicians, nurses, dentists, veterinarians, acupuncturists, massage therapists, social workers, and others; but all addicted HPs share the problem of substance abuse. Physicians have been studied the most; however, much of what is said about physicians applies to all HPs (Storr et al., 2000).

TERMINOLOGY

Historically, the word *impaired*, as in *impaired physician* or *impaired pharmacist*, became synonymous with *substance abusing*. This terminology is inaccurate because *impaired* actually means that one is unable to work with skill and safety. There are many causes for impairment unrelated to substance abuse (e.g., neurologic disorders, aging, psychiatric disorders, physical disability, or fatigue). Additionally, many HPs who have substance use disorders are not impaired at work, which is often the last place symptoms of addiction appear. Therefore, the word *impaired* should be limited to work-related impairment rather than used as a synonym for substance abuse.

EPIDEMIOLOGY

Substance use disorders (SUDs) are surprisingly common among physicians and other HPs. The lifetime prevalence among physicians is approximately 10–15 percent, similar to or slightly higher than the general population (Brewster, 1986; Talbott, 1987; Hughes et al., 1992b; Flaherty & Richmond, 1993). Nurses have a similar lifetime prevalence (Dunn, 2005). Physicians drink more alcohol than the general population, as do other members of higher socioeconomic groups. Substance abuse, disguised as *self-medication*, is especially common among physicians. As many as 11.4 percent of physicians have used benzodiazepines, and 17.6 percent have used opioids without valid prescriptions (Hughes et al., 1992b). Unauthorized use of prescription medications and alcohol abuse often begin in medical school, at an age when other groups also experience peak onset of substance use. In one study 18 percent of students met criteria for alcohol abuse in the first two years of medical school (Clark et al., 1987). Alcohol and drug-related problems account for 14 to 21 percent of all disciplinary actions by state licensing boards (Morrison et al., 1998). This does not include most HPs receiving confidential assistance for SUDs offered by physician health programs (PHPs).

GENDER

Among physicians with SUDs, males predominate 7 to 1 (McAuliffe et al., 1991). Female physicians are more likely to be younger and have medical and psychiatric comorbidity, past or current suicidal thoughts, and suicide attempts (Bissell & Jones, 1976). Interestingly, women physicians with SUDs are subject to more severe sanctions by medical boards than their male counterparts (Morrison & Wickerson, 1998).

SPECIALTY

Anesthesiologists, emergency room physicians, psychiatrists, and, in some studies, family practitioners have higher rates of SUDs than other physicians (see Table 1). Approximately 5 percent of all physicians are anesthesiologists, but they account for a disproportionately high share (13–15%) of physicians in substance abuse treatment (Talbott, 1987). The Anesthesiology Task Force on SUDs suggested that anesthesiologists have higher rates of SUDs due to the following (Berry et al., 2008):

- higher addictive potential of anesthetic drugs, such as fentanyl/sufentanil
- ease of diverting small doses of highly potent fentanyl for illicit use;
- easy access to drugs
- being accustomed to giving large doses of mood-altering, parenteral substances with immediate results
- lack of "needle taboo"
- expectation of being in control
- curiosity about what drugs feel like for the patients
- more rapid identification of SUDs, because use of highly potent drugs is more obvious
- vigilance of specialty looking for addiction within itself

Authors of study	Type of study	Number of subjects studied	Over-represented specialties	Under-represented specialties
Bissell	Closed Survey	98	Psychiatry, Emergency Medicine	Surgery
Earley and Weaver	Treatment Records	618	Anesthesiology, Emergency Medicine	Pathology, Pediatrics, Radiology
Hughes	Survey	1785	Psychiatry, Emergency Medicine	Pediatrics, Pathology, Surgery
Ikeda and Pelton	PHP/MB*	247	Anesthesiology, Emergency Medicine, Family Practice	
Knight	PHP/MB*	120	Anesthesiology, Emergency Medicine	Pediatrics
McAullife et al.	Survey	489	Psychiatry, Anesthesiology	
Meyers and Weiss	Resident Survey	1805	Psychiatry, Anesthesiology	Community health, Emergency Medicine, Surgery, Pediatrics
Morrison and Wickersham	PHP/MB*	375	Anesthesiology, Psychiatry	Internal Medicine, Pediatrics
Shore	PHP/MB*	34	Psychiatry	
Talbott	Treatment Records	1000	Anesthesiology, Family Medicine / General Practice	

*Physician Health Program/Medical Board.

Table 1. Addiction rate by specialty. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

In addition to these factors, an important debate rages about whether opioid-addicted anesthesiologists should ever return to the operating room. An early study showed poor outcomes for addicted anesthesiologists in training, reporting only 34 percent successful re-entry for those using parenteral opioids and 26 deaths (14% of the 180 reported cases), half attributed to drug relapse (Menk et al., 1990, p. 3060). This oft-quoted study potentiated a pessimistic view about anesthesiologists returning to work. It has been criticized, however, because it was an opinion survey of program directors rather than a longitudinal study. A similar survey study by Collins (2005) of anesthesiology program directors reported comparable findings, noting a smaller but still significant number (9%) of anesthesiologists in training who died from substance abuse relapses (p. 1460). By contrast, longitudinal studies report far better outcomes. California's PHP (California Diversion Program) reported a 10-year follow-up involving all 255 physician participants that showed no difference in relapse rates for anesthesiologists (Pelton & Ikeda, 1991, p. 429). Paris and Canavan (1999) compared 32 addicted anesthesiologists with 36 addicted non-anesthesiologist controls for an average of 7.5 years and showed no difference in relapse rates (p. 6). Domino and colleagues (2005) found no statistical difference in outcomes for the anesthesiologists and, strikingly, not a single episode of patient harm or anesthesiologist overdose death (pp. 1457–1458). Long-term follow-up studies of groups of physicians have shown no difference in outcome between anesthesiologists and other physicians. It appears the pessimism regarding anesthesiologists returning to work may not be warranted, although careful monitoring for early detection and deterrence of relapse is required.

DRUGS ABUSED

Alcohol is the most common substance of abuse by physicians, followed closely by opioids (Domino et al., 2005; Hughes et al., 1992b, 1999; Lutsky et al., 1993; McAuliffe et al., 1986, 1991; Talbott, 1981). Interestingly, family practice and OBGYN specialists have a

higher probability of abusing less potent opioids (i.e., hydrocodone, oxycodone, codeine, and other oral opioids) (Hughes et al., 1992a).

Exposure to, and availability of, drugs in the workplace predisposes to abuse of that drug (Hughes et al., 1999). For example, cocaine-using professions (ophthalmology, head and neck surgery, plastic surgery, and otolaryngology) have higher rates of cocaine abuse (Hughes et al., 1999). To underline this point, when surgery residents abuse cocaine, it often comes from hospital sources. Similarly, psychiatrists have higher rates of benzodiazepine abuse, 26.3 percent using benzodiazepines in the past year compared with 11.4 percent by other physicians (Hyde et al., 1995, p. 30). Nonprescription drugs, such as heroin and marijuana, contribute minimally to use pattern among physicians (Hughes et al., 1992b).

Skipper and colleagues (2004), writing about emerging abuse of tramadol among HPs, hypothesized that physicians may be the "point men" (i.e., the first) to abuse newly introduced pharmaceutical drugs. This has certainly been the case historically for opioids such as morphine, meperidine, pentazocine, butorphanol, and others. Physicians also have earlier access to unusual addictive drugs, such as propofol (Wischmeyer et al., 2007) or ketamine (Moore & Bostwick, 1999).

ETIOLOGY

Drug Access. Availability is a key factor preceding drug use in any population, including physicians. Despite ethical codes and state laws prohibiting self-prescribing, it is a common practice (Valliant et al., 1972). The particular drugs abused change over time due largely to changing patterns of availability. Hughes et al. (1992b) noted that many physicians began abusing benzodiazepines and opioids immediately after receiving their own prescribing privileges. Demerol, once the most commonly abused opioid (Talbott, 1987), dropped to 10 percent by 2004 as hydrocodone became the most frequent (40%) (Skipper et al., 2004, p. 1818).

Personality. Personality and character disorders are often consequences of drug use rather than causes of addiction. Nevertheless, certain personality factors may place physicians at risk for addictive diseases. "Sensation seeking" (McAullife, 1986), novelty seeking, intense experience seeking (Hughes et al., 1999), perfectionism, and high class rank (Bissell & Jones, 1976), "emotionally barren childhood" (Vaillant et al., 1972), childhood parental deprivation (Johnson & Connolly, 1981), sense of omnipotence or invulnerability regarding drug use, and knowledge of pharmacology may all be important risk factors for substance abuse among physicians.

Stress and Emotional Issues. Physicians in treatment for SUDs report that the stress of medical school, combined with social isolation and a lack of support, provided the backdrop for the development of addiction. They are taught in medical school and residency (and often in their childhoods) at all costs to appear in control and competent. The addiction undermines the physician's external appearance of competence. A physician falling deeper into addiction becomes more secretive and dishonest. Emotional regression and dysregulation are intensified by the secrecy and escalating stress.

CO-OCCURRING DISORDERS

Psychiatric. As in the general population, emotional and psychiatric problems appear with higher frequency in relation to substance abuse disorders, both as cause and result of substance abuse. Psychiatric problems, including depression, anxiety (including obsessive-compulsive disorder), and bipolar disorders are seen as frequently in addicted physicians as in other addicted groups. In recent years identified psychiatric comorbidity has increased, likely due to more careful evaluation rather than increased prevalence (Angres et al., 2003).

Chronic Pain. PHPs report working with an increasing number of physicians suffering from chronic pain. These cases pose diagnostic, treatment, and management difficulties. Regulatory enigmas further cloud the pain treatment of addicted physicians. Should a formerly addicted physician on opioids for pain be allowed to practice? If not, should any physician on opioids be allowed to practice? These can be perplexing questions.

IDENTIFICATION AND MANAGEMENT

Identification. Substance abuse is detected over a broad spectrum of symptom severity, from a self-report of alcoholism while in couple's therapy to

finding a physician unconscious or dead on the operating room floor. Physicians with SUDs have often had years of familial and social discord while struggling to maintain acceptable work performance. In addition, families (and medical partners) often codependently protect the addicted income earner. As soon as symptoms of substance abuse appear at work, the addiction is usually advanced. Denial, shame, and fear of reprisal often keep the HP from seeking needed care until significant external consequences occur (Centrella, 1994).

A confidential and effective PHP promotes early reporting and protects public health by offering physicians a safe haven for confronting substance abuse problems. By contrast, some patient advocacy groups claim that all HPs with a history of SUDs should be publicly identified. Most experts in physicians' health, however, believe that confidential PHPs promote early identification as opposed to the alternative, in which public stigma causes substance abusing physicians to hide their problems until disasters occur.

Other factors that work in concert with PHPs to encourage early reporting include the establishment in 2001 of new standards for physician health awareness by hospital accrediting agencies. Additionally, many states have *snitch laws* that require peers to report substance-abusing colleagues. PHPs collaborate with hospitals and rely on these laws, combined with their rehabilitative non-punitive approaches, to motivate early reporting that ultimately protects both patients and physicians alike.

Intervention. PHPs have become skilled at conducting professional interventions, often by telephone. Using the telephone for interventions may be actually less threatening and more practical. The immediate goal of the intervention is to get the HP to stop working and into an evaluation program. An HP who resists is informed that failure to comply will very likely result in a report to the regulatory board. PHP staff, often recovering HPs themselves, become skilled at gently coercing their troubled colleagues into needed evaluations.

Evaluation. Most PHPs utilize independent expert evaluation teams, selected for their credibility with the HP and with the regulatory board, which may later become involved. Most PHPs have established criteria and maintain an authorized list of evaluators (see Table 2). The opportunity for a thorough evaluation is uniquely valuable and, if mismanaged, can result in failure of the entire process.

Ideally, at the conclusion of evaluation, recommendations are presented to the HP patient in a formal meeting. Family members, particularly spouses, are commonly involved, as are PHP personnel. Such secondary interventions decrease confusion and "splitting" regarding the final recommendations. PHP personnel can answer questions about alternatives or consequences of noncompliance with evaluation recommendations. Finally, the evaluation team sends a written, comprehensive, integrated report to the PHP and other relevant parties, such as the referring hospital, if necessary.

Physicians as Patients. Treatment of physicians can be difficult, so good boundaries and experience are critical (Graham, 1980; Howard, 1983; Nace, 1995). Typically, physicians resist becoming patients, seek general medical check-ups and consultation visits less often than controls, and wait longer before seeking consultation for serious symptoms (Edelstein, 1984). They tend to diagnose and treat themselves, request "hallway" medical consultations regarding symptoms, get treatment from professional friends, and receive less than objective medical treatment. All of these factors inhibit an ill or impaired physician from seeking timely and effective treatment (Stoudemire & Rhoads, 1983).

Treatment. Approximately a dozen addiction treatment programs in the U.S. have extensive experience and recognized expertise in treating addicted physicians. These programs usually have a full-time medical director, a highly sophisticated capability for evaluation, expertise and familiarity with PHPs and Licensing Boards, and specialized treatment components for HPs, such as groups where return-to-work issues are discussed (Skipper, 1997). In many ways these are model programs for what substance abuse treatment should be for everyone.

Because the initial treatment is typically long-term (6–12 weeks), and requires the physician to be off work, some think of treatment as limited to acute episodes. When physicians leave the treatment setting, whether outpatient or residential, three weeks or six months later and return to work, the PHP vernacular is that they have completed treatment. For the next five

Component	Component type	Purpose of component*
Addiction Medicine Evaluation	Critical	Determine existence and extent of any type of addictive disorder
Addiction Psychiatry Evaluation	Critical	Determine comorbid Axis I and II disorders that interact with the addictive disease and impede treatment
History and Physical and Review of Medical Records	Critical	Determine existence and extent of medical consequences of substance use. Evaluate comorbid medical conditions (chronic pain, etc)
Psychological testing	Critical	Correlate with psychiatric evaluation, determine interaction of personality and treatment
Neuropsychological testing	Critical	Determine if cognitive deficits exist and ultimately, the physician's ability to practice
Family assessment	Critical	Determine how the evaluatee's family of origin and current nuclear family contributes to psychological, psychiatric, and addiction problems
Collection of collateral information	Critical	Evaluate effects of addiction on the workplace, family and social life. Behavioral observations that correlate with personality problems.
Hair and Body Fluid drug testing	Critical	Correlate with addiction history from multiple sources. Determine honesty of self disclosures.
Spiritual History	Critical	Assess past involvement with spiritual and religious pursuits. Determine potential pitfalls with twelve step programs.
Forensic Interview	Suggested	Determine level of honesty on a broad base of issues
Polygraph testing	Suggested	Address honesty on key issues of the evaluatee's history (Must have a list of specific questions prepared for polygrapher)
Pain evaluation	Suggested	Determine the interaction between an acute or chronic pain disorder and the addictive process. Distinguish between pseudo-addiction and addiction
Milieu interaction	Suggested	Evaluate physician for social abilities, personality issues. Help physician enter the patient role.
Sexual issues evaluation	Suggested	Evaluate need for sexual compulsivity treatment, predator treatment, or special sexual issues therapy.

*All components of the evaluation contribute to determining if an addictive disease exists, the level of care needed, and treatment planning for eventual care.

Table 2. Suggested components of a comprehensive physician addiction assessment. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

years, however, they receive far more intense treatment than members of the general public usually receive during their primary treatment. This typically includes weekly group therapy sessions, peer support groups, aftercare groups, individual counseling or psychotherapy, self-help group attendance, drug testing, worksite monitoring reports, and more. In essence, PHP-managed treatment for health professionals actually lasts more than five years because the distinction between treatment and monitoring is blurred.

Ultimately, HPs need to receive the best possible treatment because hospitals, malpractice carriers, regulatory boards, health insurance companies, family, and friends all have high expectations for continual abstinence. Relapse for an HP can and does carry harsh consequences professionally and often within the family.

The following are important components of treatment for HPs:

1. Intensive day or residential treatment
2. Personnel experienced in setting firm limits and boundaries with physician-patients
3. Regular contact with a peer (HP) support group facilitated by a physician during assessment and/or treatment
4. Opportunity for extended treatment for patients who need additional time before returning to work (2–6 month program)
5. Comprehensive family program for family and associates
6. Availability of neuropsychiatric assessment to substantiate ability to return to work

7. Availability of staff to conduct assessments, handle treatment, and advocate for the HP to return to work
8. Personnel capable of addressing needs post-discharge (Skipper, 1997).

Most HPs have work-related triggers (e.g., drug access at work, prescription pads, or locations in the office or hospital where use occurred); therefore trigger management skills and relapse prevention plans are developed prior to discharge. HPs receive minimal pharmacological treatment for addiction. About one-third of physicians in treatment receive antidepressants. Naltrexone, an opioid-blocking drug, is occasionally used in opioid-addicted physicians.

PHYSICIAN HEALTH PROGRAMS (PHPS)

History. The physician's health movement can be traced to the founding of International Doctors in Alcoholics Anonymous (IDAA) by Clarence Pearson, MD, in 1949. IDAA grew from 24 physicians, meeting in Dr. Pearson's garage in Cape Vincent, New York, to an international organization attracting thousands of physicians. On the regulatory side, the Federation of State Medical Boards called for a model probation and rehabilitation process for addicted physicians in 1958; however, no meaningful change occurred until 1973 with the publication of the watershed article from the *Journal of the American Medicine Association* titled "The Sick Physician. Impairment by Psychiatric Disorders, including Alcoholism and Drug Dependence" (Council on Mental Health, 1973). The AMA held its first conference on physician impairment in 1975. State medical societies organized committees on physician impairment, resulting in the state-by-state emergence of PHPs. Currently, all but two states in the U.S. have a formal PHP, ranging in size from one employee and a $20,000 budget to a $1.5 million budget and 19 full-time employees. Over 9,000 physicians are now in monitoring in the United States. (Skipper et al., 2004, p. 1818). Although most PHPs (85%) address other psychiatric disorders and disruptive behavior, SUDs remain the most common problems.

Education and Referral. PHPs strongly emphasize education aimed at early detection of all impairments, not just SUDs. Educational programs afford PHP staff the opportunity to network with medical leadership throughout their state. Public relations/training efforts help individuals and institutions understand and trust PHPs, which in turn promotes early referral of potentially impaired HPs.

Abstinence Monitoring. Monitoring has become more sophisticated in recent years and includes hair testing, flexible variations in drug testing panels, new markers for alcohol, medical devices to detect alcohol exposure, and software to track results more efficiently. All PHPs use random drug testing (most frequently, urine testing, but at times hair, saliva, sweat, or blood analysis). Screens commonly taper in frequency over the course of monitoring, for a period of five or more years.

Drug testing in physician populations requires considerable expertise, resourcefulness, and accuracy. Addicted physicians can use their knowledge to evade detection. Most drug panels test for 20 to 25 drugs, including a wide variety of opioids and other prescribed controlled substances (Skipper et al., 2004). Observed collection at the lab is often required to reduce the risk of cheating. Some PHPs perform periodic hair or saliva tests because these tests are less vulnerable to deception. Special screenings for fentanyl are necessary for some recovering physicians. Hair testing for fentanyl is best as these anesthesia drugs have very brief half-lives, but are readily detected in hair. Because physicians occasionally abuse more unusual drugs (e.g., ketamine, propofol, or dextromethorphan) personalized drug test panels are sometimes necessary.

In 2002 PHPs began using ethylglucuronide (EtG), a metabolite of alcohol that persists for several days or more after drinking, for early detection and deterrence of alcohol relapse (Skipper et al., 2004). Previous tests for alcohol use were inadequate due to the short half-life of alcohol in the body. Negative EtG tests, often better proof of abstinence, are needed before HPs return to work. One problem with EtG testing, however, is false-positives. The test cannot differentiate drinking from incidental alcohol exposure to various foods, hygiene products, over-the-counter medications, or topical products containing alcohol (especially if excessive alcohol vapors are inadvertently inhaled). Thus, HPs under EtG monitoring must avoid exposure to products containing alcohol, and PHPs must use care in interpreting low positive EtG results.

Recovery Support. In addition to drug testing, PHPs utilize group-facilitated psychotherapy (Caduceus groups, similar to twelve-step meetings). Unlike Alcoholics Anonymous meetings, direct feedback (*cross-talk*) is encouraged. Newcomers often obtain sponsors or guidance from Caduceus members. In one survey, "A.A. was perceived by respondents as the most potent element of their recovery" (Galanter et al., 1990, p. 63). Most PHP treatment programs strongly encourage or require Alcoholics Anonymous or Narcotics Anonymous attendance.

Relapse Management. Some PHPs have formalized models of assessing relapse with categories based upon severity:

- Level I relapse consists of missing therapy meetings, support groups, or engaging in dishonesty or other behavioral infractions (without relapse to substance use).
- Level II relapse involves use of unauthorized drugs or alcohol, but outside the context of medical practice.
- Level III relapse involves drug or alcohol use within the context of medical practice with potential risk to patients.

If managed properly, singular episodes of relapse, detected early, are not necessarily indicators of failed treatment. Unfortunately, consequences of relapse can be severe for physicians, including loss of license, arrest, and damage to professional reputation. Once a physician is in monitoring, patients run little risk even if relapse occurs, because under the careful scrutiny of PHPs, relapse is rapidly detected. Ultimately, even relapsing PHP participants have excellent long-term prognoses.

Typical responses to a relapse include:

- Reevaluation by an addiction specialist to identify the cause and suggest remedial actions to prevent future relapses
- Reexamination of the HP'S psychiatric status for psychiatric disorder, character disorder, or past unresolved trauma
- Reassessment of HP'S family dynamics and physician's support system
- Evaluation of the physician's ability to practice
- Determination of the need to repeat primary residential treatment (or to treat other elements of the addiction).

HPs who have difficulty maintaining abstinence are often removed from the workforce for extended periods until treatment providers are confident that they can safely practice. The physician's treatment provider and the monitoring PHP decide when a physician can return to work. The medical board and the public at large place pressure on all parties, so great care must be exercised in returning substance abusing HPs to work.

Outcomes. Physicians have been the subject of multiple outcome studies. Success rates have been remarkably high (Gallegos et al., 1992), with good outcomes for 91 percent over five years (Ganley et al., 2005, pp. 10–11), and low relapse rates of 25 percent (Domino et al., 2005, p. 1458) and 21 percent defined as *any* unauthorized substance use. Long-term monitoring with random drug testing under a signed PHP contingency contract may be the most important procedure accounting for their high success rates. Satisfaction surveys of PHPs by participants have generally been favorable (Fletcher & Ronis, 2005).

CONCLUSION

By utilizing the highest level of evaluation and treatment and by careful long-term monitoring with meaningful consequences for noncompliance or relapse, the nation's PHPs have achieved excellent outcomes with reduced risk to patients. PHPs are distinctive programs of care management that actively pursue early detection of SUDs prior to overt impairment at work and have high success rates with very low risk to patients, and thus should be supported.

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GREGORY E. SKIPPER
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PLANTS, DRUGS FROM. Humans have used their local plants for medicinal effects since prehistoric times. They gathered and ate plants and noticed the effects that some offered—whether therapeutic, mind-altering, or toxic. From trial and error they fashioned associations between cause and effect, keeping certain mushrooms, roots, barks, leaves, or berries for certain situations—the treatment of accidents, ill health, childbirth, coughs, fevers, rashes, and so on. Over the centuries, people established herbal medicine, as it is now called; they had also found certain plants that produced immediate and mind-altering effects, many of which were relegated to religious ritual. By the nineteenth century, Europeans had developed the science of chemistry to the point at which they could isolate and concentrate the activator in many plants.

If experimentation with plant materials has led to such cures as quinine for malaria or digitalis for heart disease, it has also led to the discovery of unpleasant effects or the discovery of poisons. From the literally thousands of substances that have been self-administered over the centuries,

only a few continue to be used for nonmedicinal purposes. Even fewer have given rise to serious problems of chronic use and dependence. The legal and readily available drugs that are found naturally in plants (e.g., nicotine, caffeine) or are derived from plants (e.g., alcohol) will be described here first because the use and abuse of these drugs is more widespread than all the other abused drugs combined. The health problems associated with the chronic use of alcohol and tobacco are therefore a very serious problem in our society, not only because of the large number of people who suffer and die each year from the direct toxic effects of these drugs but also because of the costs—the absenteeism from work and the unnecessary health care costs. The illegal drugs will be discussed next; although the illicit use of marijuana, cocaine, opioids, and psychedelics remains a major social, legal, financial, and health problem in the United States today, the proportion of the population physically dependent on these drugs is actually relatively low—only a small fraction of a percent. Finally, it is important to note that people often do not restrict their drug use to a single type. Alcohol users typically smoke cigarettes and may sometimes use other drugs as well. Heroin users may also smoke and consume alcohol, marijuana, coffee or colas, and in some instances various stimulants. Multiple drug use is therefore a relatively common occurrence.

ALCOHOL

Alcohol is perhaps the most widespread drug in use worldwide. It forms naturally by the fermentation process of plant materials and has been produced on purpose since at least Neolithic times, when grains were first farmed, harvested, stored, and processed into gruels, porridges, puddings, and so forth. Often these spoiled, forming a fermented base. Alcohol is made as well from other starchy or sugary plant materials, such as fruits, canes, roots, and such. Fermentation (also called anaerobic respiration, or glycolysis) is the chemical process by which living cells, such as yeast, use sugar in the absence of air to produce part or even all of their energy requirements. In fermentation, sugar molecules are converted to alcohol and lactic acid. Beer, wine, and cheese production, as well as certain modern commercial processes, require fermentation by specific kinds of yeast, bacteria, and molds.

Ethyl alcohol, also called ethanol, is the type of alcohol that is usually produced for human consumption. In its pure form, alcohol is a clear liquid with little odor. People drink it primarily in three kinds of beverages: (1) beers, which are made from grains through brewing and fermentation and normally contain from 3 to 8 percent alcohol; (2) wines, which are fermented from fruits, such as grapes, and naturally contain from 8 to 12 percent alcohol (up to 21% when fortified by adding more ethanol); (3) beverages or spirits, which are distilled from a fermented base, such as whiskey, gin, or vodka. Spirits contain about 40 to 50 percent alcohol, on average (often expressed in proof, so that 40% equals 80 proof; 50% is 100 proof).

NICOTINE AND TOBACCO

Tobacco is a tall herbaceous plant, the leaves of which are harvested, cured, and rolled into cigars, shredded for use in cigarettes and pipes, and processed for chewing or snuff. Tobacco has become a commercial crop in almost all tropical countries as well as in many temperate ones. The main source of commercial tobacco is *Nicotiana tabacum*, although *Nicotiana rustica* is also grown and is used in Asian tobaccos. Tobacco has been developed to yield a wide range of morphologically different types, from the small-leaved aromatic tobaccos to the large broad-leaved cigar tobaccos. Tobacco is native to South America, where it was used in a drink for ritual purposes long before inhaling the smoke of the dried plant material was first documented by the Maya more than 2,000 years ago. Tobacco was then traded and grown in Central America; it moved into Mexico and the Caribbean and eventually into North America by about 800 CE. The Arawaks of the Caribbean smoked tobacco; during Columbus's voyage of 1492, he found the Arawaks smoking loosely rolled cigars. The Spanish took tobacco seeds to Europe, where Jean Nicot, France's ambassador to Portugal, sent tobacco to Paris in 1560 and gave the plant the name of its genus (*Nicotiana*). In England, Sir Walter Raleigh began the popularization of pipe smoking in 1586, and the cultivation and consumption of tobacco spread with each voyage of discovery from Europe. Two kinds of tobacco were traded between Europe and America: "Spanish," from the West Indies and South America, and "Virginia," from the British plantations in their

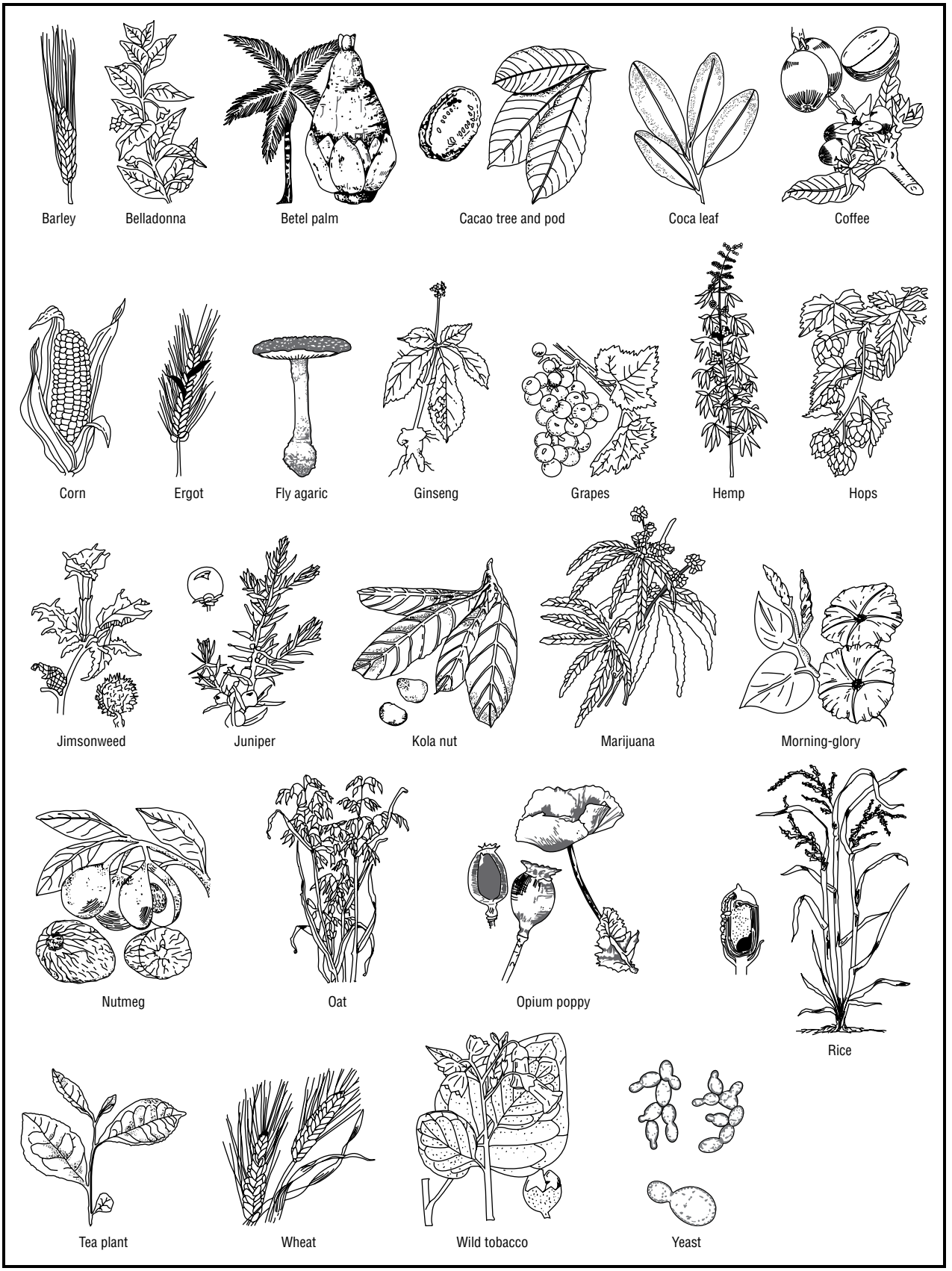

Figure 1. Some of the plants used in making drugs and alcoholic beverages. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

colony of Virginia. Despite its popularity in England, King James I forbade its production there since he vehemently disapproved of tobacco. Europeans at first smoked their tobacco in pipes, and later in cigars. It was often provided free to drinkers of coffee in coffee houses and cafés, as was the new product sugar. (Both remain strongly associated with coffee drinking.) Cigarettes spread in popularity only after the Crimean War (1854–1856), and their spread was especially aided by the first cigarette-making machine, developed in the United States in 1881.

Nicotine is the most powerful ingredient of the tobacco plant, found primarily in the leaves. Nicotine is an extremely poisonous, colorless, oily alkaloid that turns brown upon exposure to air. Nicotine can affect the central nervous system, resulting in respiratory failure and general paralysis. Nicotine can also be absorbed through the skin. Only two to three drops—less than 50 milligrams—of the pure alkaloid placed on the tongue can be rapidly fatal to an adult. A typical cigarette contains 15 to 20 milligrams of nicotine; however, the actual amount that reaches the bloodstream (and therefore the brain) through normal smoking is only about 1 milligram. Nicotine is responsible for most of the short-term as well as the long-term effects of smoking and plays a major role in the reinforcing properties.

CAFFEINE

Caffeine is an odorless, slightly bitter, alkaloid chemical found in coffee beans, tea leaves, and kola nuts, and several other plants used by humans such as cacao (chocolate) and maté (a South American holly used as a popular drink). In small amounts, caffeine acts as a mild stimulant and is harmless to most people. In large amounts, however, caffeine can result in insomnia, restlessness, and cardiac irregularities.

Tea. Tea is the beverage made when the processed leaves of the tea plant are infused with boiling water. Native to Southeast Asia, the tea plant, *Camellia sinensis*, is a small shrub-like evergreen tree that belongs to the family Theaceae. The seeds of the tea plant contain a volatile oil, and its leaves contain the chemicals caffeine and tannin. Although second to coffee in commercial value, tea ranks first as the most frequently consumed beverage. More than 50 percent of the world's population drink some form of tea every day. Many also use tea medicinally as a stimulant. The tea plant originated in the region encompassing Tibet, western China, and northern India. According to ancient Chinese legend, the emperor Shen-Nung learned how to brew the beverage in 2737 BCE, when a few leaves from the plant accidentally fell into water he was boiling. Tea leaves began to be processed in China (dried, smoked, fermented, pressed, etc.) and were sold in cakes of steamed leaves, as powder, or in leaf form. Tea was introduced by Chinese Buddhist monks into Japan (9th to 13th centuries), where the preparation and consumption of tea developed into the ritual tea ceremony called *cha no yu*. Tea culture then spread into Java, the Dutch East Indies, and other tropical and subtropical areas. British merchants formed the East India Company (1600–1858) and introduced teas from China and India into England, the American colonies, and throughout the British Empire.

Coffee. The coffee bean is the world's most valuable legal agricultural commodity. In 1982, for example, the coffee-importing bill for the United States alone was 2.537 billion dollars. Of the many varieties of the genus *Coffea* (family Rubiaceae) known to exist, only two species have significant commercial importance—*C. arabica* and *C. robusta* together constitute 99 percent of production. Coffee is native to the Ethiopian highlands and has been cultivated and brewed in Arab countries for centuries. The drink was introduced into Europe in the mid-seventeenth century and European colonial plantations were established in Indonesia, the West Indies, and Brazil, soon making coffee cultivation an important element in imperialist economies. Today, Latin America and Africa produce most of the world's coffee. The United States is the largest importer, having broken with the British tea tradition during the Revolutionary War to maintain the new American drink of coffee instead (purchased from non-British sources). In 2006 the United States imported 24 million bags of coffee, 25 percent of the world's supply.

MARIJUANA

Marijuana is the common name given to any drug preparation derived from the hemp plant, *Cannabis sativa*. Two varieties of this plant are *Cannabis*

sativa variety *indica* and variety *americana*. The several forms of this drug are known by various names throughout the world, such as *kif* in Morocco, *dagga* in South America, and *ganja* in India. Hashish refers to a dried resinous substance collected from the flowering tops of the plant (also known as *charas* in Asia). In Western culture, cannabis preparations have acquired a variety of slang names, including grass, pot, tea, reefer, weed, and Mary Jane or MJ. Cannabis has been smoked, eaten in baked goods, and drunk in beverages. In Western cultures, marijuana is prepared most often from the dried leaves and flowering shoots of the plant as a tobaccolike mixture that is smoked in a pipe or rolled into a cigarette. As one of the oldest known drugs, cannabis was acknowledged as early as 2700 BCE in a Chinese manuscript. Throughout the centuries, it has been used both medicinally and as an intoxicant. The major psychoactive component of this drug, however, was not known until the mid-1960s. This ingredient is tetrahydro-cannabinol, commonly known as THC. Psychoactive compounds (cannabinoids) are found in all parts of the male and female plants, with the greatest concentrations found in the flowering tops. The content of these compounds varies greatly from plant to plant, depending on genetic and environmental factors.

COCAINE

Cocaine is an alkaloid drug found in the leaves of the coca plant, the common name of a shrub, *Erythroxylum coca*, of the coca family, Erythroxylaceae. Coca is densely leaved and grows to heights of 8 feet (2.5 m). It is cultivated in its native South America but also in Africa, Southeast Asia, and Australia for the narcotic alkaloids of its leaves, particularly cocaine. Whole or powdered dried leaves, usually mixed with lime (calcium carbonate), have been chewed by the people of what is now Colombia, Bolivia, and Peru for centuries, to dull the sense of hunger and to lessen fatigue. The coca shrub should not be confused with the cacao tree, the source of cocoa and chocolate.

Cocaine was first used in Western medicine as a local anesthetic. In 1884 it was used by Carl Koller, an ophthalmologic surgeon. Historically, the chief medical use for cocaine has been as a local anesthetic, especially for the nose, throat, and cornea, because of its effectiveness in depressing nerve endings. Cocaine has been largely replaced by less toxic, synthetic local anesthetics. Used systemically, cocaine stimulates the central nervous system, producing feelings of excitation, elation, well-being, enhanced physical strength and mental capacity, and a lessened sense of fatigue. It also results, however, in increases in heart rate, blood pressure, and temperature, and its use can result in death. Cocaine use became popular because of its stimulating properties. In Western countries, it is frequently ingested by sniffing its fine white powder, often called snow. It is sometimes injected intravenously, although repeated injections can result in skin abscesses, hepatitis, and the spread of AIDS. Cocaine can also be inhaled (smoked) once it has been converted to its freebase form; some preparations of freebase cocaine are known as rock or crack. Crack cocaine gained popularity in the late 1980s and early 1990s because it is relatively inexpensive as a single dose, (e.g., $10 to $20 per "hit"); usually smoked in a special pipe, it produces an intense euphoria as it is rapidly absorbed from the lungs and carried by the blood directly to the brain.

OPIUM

Opium is a drug obtained from the juice of the immature seed pods of the oriental poppy, *Papaver somniferum*. There are over 20 natural alkaloids of opium, including codeine and morphine. Morphine is the largest component and it contributes most significantly to opium's physiological effects. Heroin (diacetylmorphine) was derived from morphine and is the most important drug synthesized from opium's natural alkaloids. As a folk medicine, opium has been used to relieve pain, reduce such drives as hunger and thirst, induce sleep, and ease anxiety and depression. Opium and some of its derivatives are highly addictive, and their use has led to abuse and serious drug problems. Drugs derived from opium are still used widely in medicine, despite the development of such synthetic opioid drugs as meperidine (Demerol). The therapeutic effects of the opioids include pain relief, suppression of the cough reflex, slowing of respiration, and slowing of the action of the gastrointestinal tract. Opium's constipating effect led to its initial use, in the form of paregoric, in treating diarrheas and dysenteries. The main producers and exporters of opium are located in India and Turkey. About 750 tons (680 metric tons) of opium are annually needed to meet medical uses worldwide.

Opioids have been used since ancient times both for medicinal purposes and for pleasure. Opium was taken orally as a pill or added to beverages for centuries in the Middle East, India, and Asia. Addiction did not become a widespread problem until the practice of opium smoking was introduced by the British from India into China in the late seventeenth century (in an effort to gain a trade opening to the "closed" empire of China). China attempted to deal with the problem by restricting the cultivation and importation of opium in the nineteenth century. This restriction led to the Opium Wars (1839–1842), since the opium trade became highly profitable to the British East India Company. Britain won over China, and opium was sold to the Chinese through treaty ports until the twentieth century.

In Europe and North America in the eighteenth century, opioids became widely used as most effective and reliable analgesics (painkillers). Heroin was developed in Germany in the 1890s and used from 1898 as a cough suppressant and analgesic with the hope that it would not lead to addiction, as did morphine (from which it was derived). From the first year or two after introduction, some clinicians agreed that it did not show addictive properties. A few even suggested that it might be useful in treating people addicted to morphine. Within a few years it became clear that, like morphine, the use of heroin could lead to addiction comparable in gravity to that of morphine.

On the street, opium is sold as a dark brown chunk of gum (from the pod of the opium poppy) or in dried powdered form. It is smoked, eaten, and drunk or injected as a solution for medicinal and recreational purposes. Indian and Chinese immigrants brought the practices with them, but the number of users is not great. During the early phases of addiction, opium produces a feeling of euphoria or well-being. With time, one may become dependent through physical and emotional factors. Tolerance develops and larger and larger doses of the drug are required to produce the same effect. If denied access to the drug, an addict will experience severe withdrawal symptoms; sudden withdrawal in a heavily dependent person has occasionally been fatal.

MESCALINE

Peyote, or mescal, is the common name of the small spineless cactus *Lophophora williamsii*, found in the southwestern United States and northcentral Mexico. Peyote is used in Native American religious rituals, primarily for its hallucinogenic effects. At the end of the nineteenth century, Arthur Heffter demonstrated that mescaline (3,4,5-trimethoxyphenethylamine) is responsible for peyote's pharmacological effects. Mescaline is related to the amphetamines. When ingested, it can produce hallucinations, frequently of a visual nature, characterized by vivid colors, designs, and a distorted space perception. It stimulates the autonomic nervous system and can cause nausea, vomiting, sweating, tachycardia (rapid heartbeat), pupillary dilation, and anxiety. The use of peyote in Native American ritual, referred to as Peyotism, was documented by Europeans in the sixteenth century. The modern practice of the peyote-based religion began in the late nineteenth century, was widely practiced by Native Americans in the southwestern United States, and was incorporated as the Native American Church in 1918. This church claimed more than 200,000 members in the 1960s. From the church member's point of view, peyote symbolizes spiritual power; the peyote "button"—the dried top of the cactus—is eaten as a sacrament to induce a hallucinogenic trance (of a few hours duration) for communion with God.

PSILOCYBIN

Psilocybin is the active substance contained in the fruiting bodies of the *Psilocybe mexicana* mushroom (called the magic mushroom); it is a potent hallucinogen that can cause psychological disturbances. Taken orally or injected, the drug produces effects similar to those of the chemically unrelated LSD (lysergic acid diethylamide), and cross-tolerance has been experienced between psilocybin, LSD, and mescaline. The use of psilocybin is illegal in the United States, except for the direct consumption of mushrooms by a few religious groups as part of their ritual.

OTHER SUBSTANCES

Throughout the world, many other natural plant substances are used for mind- and mood-altering effects. These include the use of the KAVA root (*Piper methysticum*) for an intoxicating drink in the South Pacific; indole-containing snuff (distilled from indigo, genus *Indigofera*) among the Amazonian Indians of Brazil; khat leaves of a bush indigenous to East Africa containing an amphetamine-

like drug (cathinone); betel nut derived from the betel palm (*Areca catechu*) and widely used throughout the Pacific rim; and fly agaric (a toxic mushroom, *Amanita muscaria*) among the Uralic-speaking tribes of Siberia.

See also **Alcohol: History of Drinking (International); Ginseng; Ibogaine; Jimsonweed; Morning Glory Seeds; Nutmeg; Opiates/Opioids; Paregoric; Tobacco: Tobacco Industry.**

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NICK E. GOEDERS

POISON. A substance that, when introduced into the body in relatively small quantities, causes destruction or malfunction of some tissues and organs. Depending on the quantity in the body (the dose), a poison can kill. The word *poison* usually implies that a substance has no healthful use and is to be considered dangerous even in small quantities. Most common household substances are poisonous, including bleach, ammonia, drain cleaners, paint supplies, and so on.

SUBSTANCES CAUSING DEATHS FROM ACCIDENTAL POISONING

DRUGS

Analgesics and antipyretics
Sedatives and hypnotics
Tranquilizers
Antidepressants
Other psychotropic agents
Other drugs acting on the nervous system
Antibiotics and other antimicrobial agents
Cardiovascular drugs
Hormones
Hematological agents
Other drugs

OTHER SUBSTANCES

Alcohols
Cleaning and polishing agents and paint
Petroleum products
Pesticides
Corrosives and caustics

GASES

Utility gas
Carbon monoxide
Nitrogen oxides
Freon
Other gases

In the practice of medicine, many useful drugs, such as antibiotics for treating infections or antihypertensive drugs for treating high blood pressure, can be poisonous or toxic in higher doses. Almost all drugs that are abused can be poisonous or toxic; some, even at relatively low doses.

A few drugs that are commonly used in medicine in small amounts to produce important therapeutic effects are also used in other contexts as poisons. For example, the drug warfarin is used medically as an anticoagulant (to increase the time it takes blood to clot), an important effect for people who have had strokes or heart-valve replacement—but warfarin is also used as rat poison, because when rats eat it in large amounts they die soon after from massive hemorrhages. The same mustard gas (nitrogen mustards) that, as poison gas, caused much death and suffering in World War I, actually has medical use in the treatment of certain leukemias. Similarly, a series of extremely potent chemicals were developed during World

War II as nerve gases for warfare, which act by flooding the body with excess acetylcholine (a body substance necessary for synaptic transmission), causing muscle paralysis and death. Consequently, close chemical relatives of some of the most potent nerve gases ever developed are being used to treat such medical disorders as myasthenia gravis, in which there is not enough acetylcholine in nerve endings.

Treatment of someone who has been poisoned may require removal of the poison from the body (e.g., with the use of a stomach pump for ingested poisons), administration of an antidote if one exists, or simply support in repairing the damage done to the body. Many cities have a telephone "hot line" or poison-control center number where information about poisons, antidotes, and actions to take in case of poisoning can be obtained; often, the staff will alert emergency medical service (EMS) units to arrive in mere minutes. In case of a poisoning, including a drug overdose, it is essential to call for expert medical help as quickly as possible to minimize damage to the victim.

See also **Complications: Medical and Behavioral Toxicity Overview; Drug Types; Inhalants.**

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POLYDRUG ABUSE. This term refers to the common observation that individuals who are considered drug abusers often abuse more than one type of drug. Almost all drug abusers smoke nicotine cigarettes and a large proportion consume alcoholic beverages, but many of them do not consider the co-occurrence of these two forms of drug use as an instance of polydrug abuse.

There are several types of polydrug abusers. They include those who abuse two or more substances but have a definite preference for one; only when they are not able to get supplies of their preferred drug do they abuse other types of drugs. These other types of drugs may be either from the same pharmacological class (e.g., heroin abusers may abuse such other narcotics as codeine or Demerol) or from different pharmacological classes (e.g., stimulant abusers—such as cocaine abusers—may also use heroin, a narcotic). Some polydrug abusers do not necessarily have a favorite drug but instead may select different drugs for consumption at different times (e.g., stimulants in the morning, sedatives at night) or under different conditions.

Polydrug abuse can also refer to the consumption of a drug to counteract an unpleasant effect produced by another drug or by withdrawal from another drug. For example, individuals who take enough stimulants to become highly agitated and aroused may take a tranquilizer to counteract the unpleasant side effects. Finally, polydrug abuse can refer to the consumption of different drugs simultaneously (e.g., speedballs). The assumption is that the different drugs in combination constitute more than the sum of their individual parts, producing a unique, highly reinforcing effect.

See also **Barbiturates; Barbiturates: Complications; Drug Abuse Warning Network (DAWN); Drug Interactions and Alcohol; Prescription Drug Abuse; Sedatives: Adverse Consequences of Chronic Use.**

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PREGNANCY AND DRUG DEPENDENCE. Drug use is most prevalent during the reproductive years. A report from the American College of Obstetricians and Gynecologists (ACOG) reported that among women age 15 to 44 nearly 90 percent have used alcohol, 4 percent have used marijuana, and 14 percent have used cocaine (ACOG, 1994). Although a reduction in substance use may

occur during pregnancy, a large number of fetuses are exposed to illicit substances in utero. Based on the Substance Abuse and Mental Health Services Administration's National Survey on Drug Use and Health (NSDUH) among pregnant women, 18 percent reported smoking tobacco, 10 percent reported drinking alcohol, and 4 percent reported using at least one illicit drug in the past month (SAMHSA, 2005). According to this survey, pregnant white women and pregnant Hispanic women had lower rates of past month illicit drug use (4.4 and 3.0%, respectively) than pregnant black women (8%). Further, the rates of illicit drug use during pregnancy were higher among women age 15 to 25 (1.6%) as compared with women age 26 to 44. From the public health perspective the impact of substance use during pregnancy extends far beyond maternal health to that of a large number of the unborn population.

Maternal prenatal substance abuse became an issue for public health debate in the mid-1980s when heightened attention came in response to the emergence of a perceived "crack" epidemic (Lester, Andreozzi & Appiah, 2004). During this time, drug use by pregnant women was seen by some as a moral as well as a public health issue. Since then, there has been an onslaught of attention and research in this area. There have been a number of large-scale studies that have examined substance use during pregnancy, including the National Institute on Drug Abuse's National Pregnancy and Health Survey, the National Center for Health Statistics' National Maternal and Health Survey, and the National Longitudinal Survey.

EXPERIENCE OF SUBSTANCE-USING PREGNANT WOMEN

Substance-using pregnant women are often stigmatized, which in turn may cause them to deny their drug use, to not acknowledge its possible harmful effects, and to not seek help. Fear of negative repercussions may limit their use of medical and social welfare systems. Women who are chronic heroin, marijuana, or cocaine abusers are often already in sufficiently poor health, compromising the growth and well-being of the fetus. The most frequently encountered medical complications in women who abuse drugs during pregnancy include anemia and various infections such as pneumonia, hepatitis, urinary tract infections, and sexually transmitted diseases. In addition, these women are at risk for infection with human immunodeficiency virus (HIV).

HIV has been increasingly linked to drug use. The practice of sharing contaminated needles to inject heroin or cocaine, the practice of prostitution in order to procure money for drugs, or the direct sex-for-drugs transaction associated with crack smoking have all contributed to this serious international health crisis. Although the exact risk of an infected mother passing the disease to her offspring is not precisely known, it is estimated that in the absence of detection and treatment, the rate of perinatal HIV transmission is approximately 25 percent (Olges et al., 2007). In addition to many potential medical problems, the lifestyle of pregnant addicts is burdensome. Associated risks include unemployment, poverty, prostitution, physical abuse, stress, depression, and lack of social support.

IMPACT ON FETAL WELFARE

Teratology is the study of perinatal developmental injury or abnormal development, and of the causative factors which include birth accidents and genetic mutations that increase the risk of developmental injury. Behavioral teratology investigates the developmental impact of exposure to exogenous agents (e.g., illicit substances) or of events during different critical periods on the developing brain, and hence, on the child's psychological development. The impact of individual exposures is assessed using varying levels of analysis (e.g., behavioral, neuropsychological, neurochemical, neuropathological) and at varying distances in time starting from the initial fetal exposure. There are ten basic principles central to behavioral teratology investigation (Mayes & Ward, 2003; Vorhees & Mollnow, 1987; Wilson, 1973, 1977):

1. Delineate the possible mechanisms of teratogenic effect.
2. Define the specific teratogenic agent.
3. Specify the timing of the exposure (there are differing windows of vulnerability in the developing fetus).
4. Define the nature of the exposure (route, amount, and duration).
5. Delineate the range of susceptibility and response relationships.
6. Select those groups at greater or lesser risk for exposure.

7. Consider the environmental context and conditions most related to the exposure.
8. Define the outcomes most likely to be related to the mechanism of action of the exposure agent or event (it may be that the context of drug abuse greatly alters the child's care giving environment).
9. Consider when exposure-related outcomes are most likely to become apparent (not all effects are apparent in the perinatal period).
10. Take into account those conditions that ameliorate or exacerbate any exposure-related functional outcomes (effects may be exacerbated or ameliorated by other exposures or environmental conditions).

Fetal exposure to illicit substance use, like other exogenous agents, is neither specific nor discrete; the outcomes are not uniformly present even with documented exposure, and the severity or extent of the deformity or developmental abnormality is variable. Abuse of one or multiple drugs rarely occurs independent of other developmentally salient variables. Parental health during pregnancy is usually compromised and more often than not, substance-using mothers receive little or no prenatal care. Exposure to nearly all illicit substances during pregnancy may at the very least influence fetal growth and contribute to intrauterine growth retardation and perhaps prematurity. Important covariates include those broadly describing postnatal parental/care-giving function. Indeed, variables such as ongoing parental substance use, neglect and abuse, parental depression, exposure to violence as witness or victim, homelessness, parental separation, and parental loss are common events for children growing up in substance-using families.

In sum, a difficulty in evaluating the effects of illicit drugs is the range of sociodemographic, psychosocial, behavioral, and biological risk factors associated with both illicit drug use and adverse pregnancy outcomes. It is challenging to determine the extent to which adverse outcomes are due to the direct effects of the drug versus the surrounding social conditions (Mayes & Ward, 2003). The accumulation of numerous risk factors appears to have a greater negative impact on child development than any single risk factor. As such, complex models that include interactions between the exposure agent and the environment are essential.

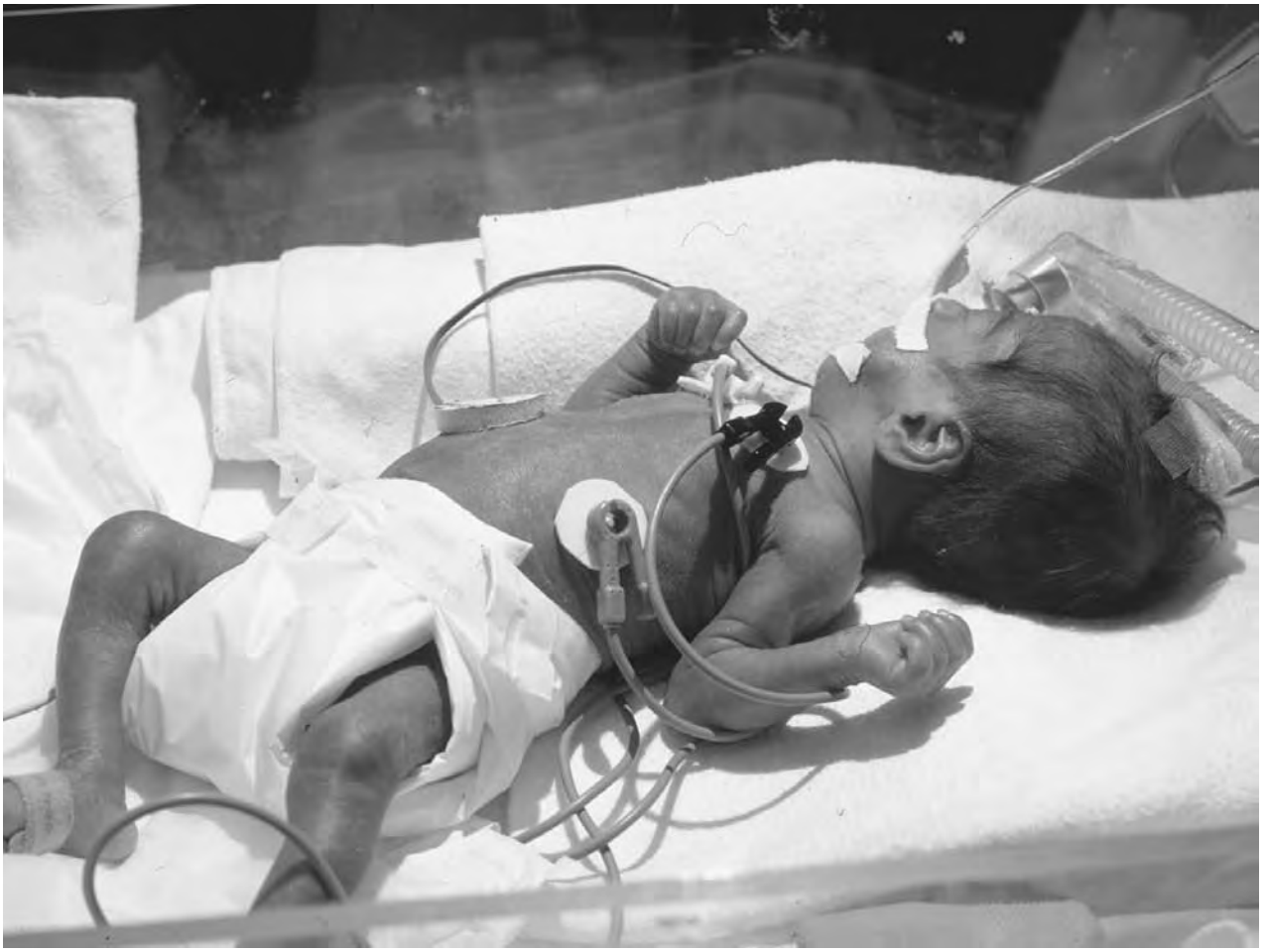
IMPACT OF OPIOIDS, COCAINE, AND MARIJUANA

Opioids. Newborns that have been prenatally exposed to opiates (heroin or methadone) are born passively addicted to the drug and exhibit withdrawal symptoms in the first days to weeks after delivery. Numerous studies have also replicated the finding that prenatal opioid exposure reduces birth weight and head circumference (e.g., Hans, 1992). Prenatal exposure to opiates also contributes significantly to an increased incidence of sudden infant death syndrome (SIDS). In some studies the incidence of SIDS is eight times that reported for non-opiate-exposed infants (Rosen & Johnson, 1982; Hans, 1992).

Neurobehavioral assessments in the newborn period found that opiate-exposed infants are more easily aroused and more irritable (Jeremy & Hans, 1985). They exhibit less time in quiet sleep compared to active sleep and show increased muscle tone and poor motor control (e.g., tremulousness and jerky movements). Opiate-exposed infants are less often in alert states and are more difficult to bring to an alert state. The dramatic neurobehavioral abnormalities seen in the newborn period generally diminish during the first month of life for the majority of infants, and are thus assumed to reflect the transitory symptoms of narcotic withdrawal rather than evidence of permanent neurological dysfunction (Jeremy & Hans, 1985).

Infancy studies have shown some persistent problems in poor motor coordination, high activity level, and poor focused attention among opiate-exposed infants in the first year of life (Hans, 1992). These state and motor regulatory difficulties make it hard for even a well-functioning adult in a relatively low-stress environment to care for the infant, and present significant problems for an opiate-addicted adult who is experiencing his or her own state and attentional regulatory difficulties.

Follow-up studies through the early childhood of opiate-exposed children compared with non-opiate-exposed children have reported few or no differences in cognitive performance. However, opiate-exposed school-age children show higher activity levels, are often impulsive with poor self-control, show poor motor coordination, and have more difficulty with tasks requiring focused attention (Wilson, 1989).



A crack-addicted baby is connected to sensors and a respirator in an incubator at Lincoln Hospital in New York. Crack-addicted babies usually exhibit irritability, nasal congestion, respiratory distress, seizures, and often have knee and nose abrasions. JOHN CHIASSON/GETTY IMAGES.

There are few studies past the years of early childhood of the long-term effects of prenatal opiate exposure. Data suggest that, by adolescence, opiate-exposed children exhibit an increased incidence of behavior and conduct problems including impulsivity, involvement in criminal activities or in early substance abuse, more antisocial behavior, and increased school dropout. It is not clear how much these problems in conduct and impulse regulation are attributable to persistent effects of prenatal opiate exposure and how much they are the consequence of cumulative exposure to the discord and dysfunction often characterizing substance-abusing households. In addition, the potential exists for these behaviors to reflect an inherited predisposition to conduct disorder and antisocial personality disorder, both of which are highly associated with substance dependence.

Cocaine. Cocaine has been studied extensively because of a rapid rise in its use during the 1980s and public concern over the purported "crack baby" phenomenon. The chemical properties of cocaine allow it to cross the placenta easily and enter the fetus. The passage from maternal circulation to the fetus is enhanced by the injection or smoking of cocaine. In addition, because of acid/base balance issues and low levels of certain enzymes, which usually metabolize the drug, accumulation of cocaine in the fetus occurs. Furthermore, the "binge" pattern commonly associated with cocaine use may lead to even higher levels of cocaine in the fetus. Transfer of cocaine appears to be greatest in the first and third trimesters of pregnancy. In the first trimester, prenatal cocaine exposure may have a direct effect on neuronal migration and brain structure formation whereas

in the third trimester the effect may be on synaptogenesis (i.e., the formation of new synapses between nerve cells) in specific brain regions (Hadeed & Siegel, 1989).

The use of cocaine by the mother may also affect the course of labor. Crack appears to directly increase contractions of the uterus and may thus precipitate the onset of premature labor. Higher rates of early fetal loss and third-trimester separations of the placenta appear to be major complications of maternal cocaine use. Increased blood pressure and increased body temperature caused by cocaine may be responsible for early fetal loss and later separation of the placenta. The latter is hazardous to the fetus and the mother because of associated bleeding, shock, and the chance of death for both, if an emergency cesarean section is not performed (Hadeed & Siegel, 1989).

In terms of outcomes it now appears that early reports that portrayed children who were exposed to cocaine in utero as irreparably doomed and damaged were exaggerated. Although still inconclusive on many crucial issues, published studies to date nonetheless reveal evidence of cocaine-related effects on the neuropsychological functions subserving arousal and attention regulation and reactivity to stressful conditions (Mayes et al., 1998). In studies of newborns and 3- to 6-month-old cocaine-exposed infants, impairments have been reported in startle-responsiveness, auditory information processing, habituation, recognition memory, and reactivity to novelty. Studies suggest persisting problems into school-age, specifically, small deficits in intelligence and academic skills including poor sustained attention, more disorganization, and less abstract thinking.

Infants prenatally exposed to cocaine are often also exposed to a number of other risk factors that may also contribute to impaired development. First, these may include exposure to other substances of abuse including alcohol and tobacco as well as opiates, marijuana, and amphetamines. Second, infants postnatally exposed to cocaine that continue to be exposed to ongoing parental substance abuse are more often neglected and abused, and they have parents who are more frequently depressed and have higher overall stress and anxiety. Adults who are under the influence of cocaine are less able to respond adequately to their children at any given age. Third, the psychological/personality factors that lead an adult to substance abuse may have genetic implications for the fetus. These factors alone or in conjunction influence the observed developmental outcomes including attentional and arousal regulatory functions, language development, and emotional regulation (Mayes & Truman, 2002).

Marijuana. After alcohol, marijuana is the most commonly abused drug in the United States, and like alcohol, marijuana abuse cuts across different socioeconomic groups and strata. Marijuana has an indirect effect on fetal oxygenation through the high level of carbon monoxide found in marijuana smoke (higher than that in cigarette smoke), which in turn results in fetal hypoxia. This type of effect may influence fetal growth, particularly in instances of heavy marijuana use.

Characteristics of newborns exposed to heavy maternal marijuana use are tremors and increased startle in the first 7 to 14 days of life (Levy & Koren, 1992). Changes in sleep patterns have also been reported. Longer-term studies of the outcome of prenatal marijuana exposure are few in number. There is limited support for an impact on IQ in childhood. Behaviorally, children exposed to marijuana prenatally may show increased impulsivity and difficulties with sustained attention (Fried et al., 1992). There is a suggestion that by early adolescence those children exposed to marijuana prenatally may have more difficulty with complex visual processing, though follow-up through adolescence is warranted to determine the course of this effect.

Each of these presumed effects relating prenatal drug exposure to neurobehavioral and developmental dysfunctions must be viewed in the context of the postnatal substance-abusing environment in which many prenatally drug-exposed children remain. As already described, postnatal drug use carries a number of risks to children's development. These include exposure to extreme, often chronic violence, virtual homelessness, poverty, parental neglect and abuse, and parental depression and associated psychopathology. Each of these factors in turn influences the parenting behaviors of adults who are also substance abusers.

AMELIORATING THE EFFECTS

There is no clear empirical evidence as to what treatment modality is best for substance-using mothers. However, there is a general consensus that providing comprehensive multidisciplinary drug-treatment services and prenatal care for addicts will significantly reduce the medical and psychological problems and the death rate in both mothers and infants (Bauer et al., 2002). Comprehensive care may include specialized treatment in a perinatal center where the mother can be provided with comprehensive addictive and obstetrical care, psychosocial counseling, and supportive services (e.g., drug abuse treatment, medical and psychiatric care, public assistance, day care, housing, and vocational counseling). Clinicians must work as part of a well-coordinated team that closely monitors mothers' and children's progress.

Specific to substance use, supportive psychotherapy typically includes counseling, group therapy, lifestyle-change training, exercise, and self-help groups such as Narcotics Anonymous. Relapse prevention methods, which use peer support and learning principles, are directed toward avoiding situations that elicit conditioned cravings for and abuse of substances and toward developing better coping skills. Selective pharmacologic therapy is an important treatment modality. A prime example is methadone, which has been widely used for years in treating opiate dependence during pregnancy. Methadone maintenance reduces the risk of relapse and enhances retention in treatment and prenatal programs. Furthermore, methadone treatment among pregnant women who are opiate-dependent has been shown to improve perinatal outcome (Dashe et al., 2002). Other forms of pharmacologic maintenance therapy are not currently accepted during pregnancy.

To target children's developmental outcomes, maternal-infant attachment should be given special emphasis. After children are born, substance abuse has the potential to disrupt parenting behavior, as the use of illicit drugs can impede awareness of and sensitivity to environmental cues, interfere with emotion regulation, judgment, and aspects of executive functioning, and impair motor skills. All of these abilities are necessary to provide stable, timely, and responsive parenting. Growing evidence suggests that the quality of care in the home environment during the first five years can have a significant impact on children's developmental outcomes such as capacities for self-regulation, autonomy, and evolving expectations for relationships. Thus, the first five years of life represent a window of opportunity within which therapeutic interventions with drug-dependent parents are critical to promote optimal child development. Programs that have demonstrated promise focus on improving the quality of the mother-child relationship. Parenting intervention in this relational approach emphasizes the emotional quality of the relationship between parent and child as the mechanism that promotes optimal child development. These interventions aim to (a) foster flexibility and emotional openness in mothers' mental representations of their children, (b) foster a greater capacity to make accurate inferences about their children's emotional needs, and (c) foster sensitive responses to children's emotional needs (Suchman et al., 2006). This focus on the emotional aspects of the care-giving relationship is critical to sustained improvements in children's long-term psychosocial development.

Care of substance-using pregnant women is complex, difficult, and often demanding. Providers must be aware of the unique psychological and social needs, and the related legal and ethical ramifications surrounding substance use during pregnancy (Lester, Andreozzi, & Appiah, 2004). The goal of comprehensive perinatal care should be to promote safe and healthy pregnancies, improve perinatal outcome, enhance the development of children exposed to illicit substances, and keep the patients from substance abuse after the pregnancy.

See also **Alcohol- and Drug-Exposed Infants; Fetal Alcohol Syndrome; Fetus, Effects of Drugs on the; Injecting Drug Users and HIV; Opioid Complications and Withdrawal; Substance Abuse and AIDS.**

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PRESCRIPTION DRUG ABUSE. Prescription drugs have become as of 2008 a major category of abused substances, and the prevalence of prescription drug abuse may soon overtake that of illicit drugs. Abuse of prescription medications may result from the inappropriate dosing or route of administration or use for reasons other than those for which the prescription is indicated. Some classes of prescription drugs act, either directly or indirectly, upon the same brain systems affected by illicit addictive drugs; therefore, their nonmedical use may result in abuse and addiction.

Prescription drug abuse may be classified under the diagnostic criteria given to substance abuse or substance dependence (addiction) patterns. Commonly abused classes of prescription drugs are opioids, central nervous system depressants, and stimulants.

OPIOIDS

Prescription opioids are commonly prescribed because of their effective pain-relieving properties, and are mostly administered orally. Morphine is often used before or after surgery to alleviate severe pain. Codeine is used for milder pain and severe coughing. Other examples of opioids that can be prescribed to alleviate pain include oxycodone (OxyContin, an oral, controlled release form of the drug), propoxyphene (Darvon), hydrocodone (Vicodin), hydromorphone (Dilaudid), and meperidine (Demerol). In addition to their effective pain-relieving properties, some medications in this class, such as diphenoxylate (Lomotil), can be used to relieve severe diarrhea.

Opioids act on the brain and body by attaching to specific proteins known as opioid receptors. These receptors are located in the central nervous system (the brain and the spinal cord), and the attachment of the prescription drug to the receptor blocks the perception of pain. In the short-term, opioids can produce drowsiness, nausea, and constipation; large, single doses may cause severe respiratory depression that can lead to death. Opioid drugs also can induce euphoria by affecting the brain regions that mediate the perception of pleasure and may be intensified when administered through nonprescribed routes. For example, OxyContin often is snorted or injected to enhance its euphoric effects. Long-term use of opioids can lead to physical dependence and addiction. Withdrawal symptoms include restlessness, insomnia, vomiting, muscle and bone pain, diarrhea, cold flashes, and involuntary leg movements. Opioids are known to interact with other substances, including those that cause central nervous system (CNS) depression (including alcohol, antihistamines, barbiturates, benzodiazepines, and general anesthetics). Since these substances slow breathing, their combined effects can lead to life-threatening respiratory depression. Options for effectively treating addiction to prescription opioids are drawn from research on treating addiction to heroin (an illicit opioid).

Pain-relieving prescription drugs are the most widely abused class. Attention was drawn to this class around 2000, following a rapid rise in the prescribing of OxyContin and reports of users crushing time-release capsules to allow for the entire dose to be dissolved quickly. In 2002, Drug Abuse Warning Network data ranked prescription opioids fourth among emergency room mentions and first among drug-associated deaths.

CENTRAL NERVOUS SYSTEM DEPRESSANTS (SEDATIVES AND TRANQUILIZERS)

CNS depressants can slow normal brain function. Because of this property, some CNS depressants, including sedatives and tranquilizers, are useful in the treatment of anxiety and sleep disorders. In higher doses, some CNS depressants can become general anesthetics. There are many CNS depressants, and most act on the brain in similar ways. This class of drugs increases the neurotransmitter gamma-aminobutyric acid (GABA), which then acts by decreasing brain activity. Although different classes of CNS depressants work in unique ways, the commonality is their ability to increase GABA activity to produce a drowsy or calming effect.

Results of short-term use of CNS depressants include initial drowsiness and a feeling of uncoordination. Effects of long-term use include the potential for physical dependence and addiction. Tolerance may occur, as larger doses may be needed to achieve therapeutic effects. When use is eventually reduced or stopped, withdrawal may occur. Because CNS depressants work by slowing the brain's activity, a potential consequence of abuse is that the brain's activity can rebound to the point that seizures can occur once the drug is discontinued. Often the abuse of CNS depressants occurs in conjunction with the abuse of another substance, such as alcohol or cocaine. When used in combination, CNS depressants may have additive effects, which can slow the heart or respiration and may be fatal. Therefore, CNS depressants should not be combined with any medication or substance that causes drowsiness, including prescription pain medicines, certain over-the-counter cold or allergy medications (which can contain alcohol or antihistamines), or beverage alcohol.

Most CNS depressants can be divided into groups, based on their chemistry and pharmacology.

Among the medications that are commonly prescribed for these purposes are barbiturates and benzodiazepines.

Barbiturates, such as mephobarbital (Mebaral) and pentobarbital sodium (Nembutal), are used to treat anxiety, tension, and sleep disorders. Although barbiturates are more or less obsolete as tranquilizers and sleeping tablets, addiction to them continues to be encountered as of 2008. Tolerance and physical dependence can rapidly occur during therapy, and abrupt withdrawal can result in a severe and life-threatening withdrawal state. Studies in abusers show them to greatly prefer barbiturates to benzodiazepines, which have replaced them pharmacologically and are discussed below. Meprobamate, a carbonate used as a tranquilizer, is similar in many ways to the barbiturates, including its abuse potential.

Clinically, patterns of nonmedical use of nonopioids vary greatly; large quantities can be injected into a vein or muscle, often producing abscess formation. Other users take large amounts by mouth, on a binge or spree basis, the most popular being pentobarbital, amylbarbital, quinalbarbital, and Tuinal, the amylbarbital/quinalbarbital combination. Some users become permanently intoxicated and totally engrossed in maintaining their supply, licit or illicit. Polydrug use, which combines these drugs with amphetamines or opioids, is common.

Withdrawal can be hazardous, with the risk of seizures or psychotic features, when discontinuing chronic usage of 500 milligrams a day or more. Withdrawal delirium (similar to delirium tremens, DTs) is common and often difficult to treat; a chronic state with hallucinations may ensue.

Benzodiazepines, such as diazepam (Valium), chlordiazepoxide (Librium), and alprazolam (Xanax), are prescribed to treat anxiety, acute stress reactions, and panic attacks. The more sedating benzodiazepines, such as triazolam (Halcion) and estazolam (ProSom) are prescribed for short-term treatment of sleep disorders. Usually, benzodiazepines are not prescribed for long-term use and therefore increasing therapeutic levels are uncommon. The benzodiazepines supplanted the barbiturates because they seemed to be at least as effective, with few side effects and less likelihood of producing addiction. However, they have been used as drugs of abuse, either as the main drug of abuse or as part of a polydrug-abuse pattern. Abusers have found that the effect of benzodiazepines is enhanced through interaction with a number of other drugs. Within polydrug abuse, the benzodiazepine is used to eke out the supply of opioid or to ease the crash from the high euphoria of cocaine use.

In the 1990s, flunitrazepam (Rohypnol) was a benzodiazepine sold as a hypnotic in many countries around the world. Reports surfaced that it was being added to the alcoholic drinks of unsuspecting women by their dates, resulting in an intoxication so profound the woman is unable to remember recent activities. It became widely known as the *date-rape drug*. In 1997, the manufacturer changed the formulation of the pill so that when it dissolves in a drink it produces a characteristic color.

A new generation of non-benzodiazepine anxiolytics (e.g., zolpidem and zaleplon) has emerged with the hopes of avoiding the difficulties that arose with benzodiazepines' abuse. While early investigations showed little evidence of abuse or dependence, several subsequent studies demonstrated that these medications do have significant abuse potential, particularly at high doses and in patients with a history of substance dependence.

STIMULANTS

Stimulants enhance brain activity, causing an increase in alertness, attention, and energy. They have also been found to raise mood, increase the sense of well-being, and decrease appetite. Stimulants historically were used to treat asthma and other respiratory problems, obesity, neurological disorders, and a variety of other ailments. As their potential for abuse and addiction became apparent, the medical use of stimulants began to wane. As of 2008, stimulants are prescribed for the treatment of only a few health conditions, including narcolepsy, attention deficit hyperactivity disorder (ADHD), and depression that has not responded to other treatments. This class of medication—which as of 2008 includes dextroamphetamine (Dexedrine and Adderall) and methylphenidate (Ritalin and Concerta)—has a chemical structure that is similar to that of a family of key brain neurotransmitters called *monoamines*, which include norepinephrine and dopamine. Stimulants enhance the effects of these chemicals in the brain. The result is increased blood pressure and heart rate, constriction of blood vessels, increased blood glucose, and an opening of the pathways of the respiratory system.

Additional short-term side effects include suppressed appetite and sleep deprivation. In addition, the increase in dopamine is associated with a sense of euphoria that can accompany the use of stimulants, sometimes resulting in dependence or addiction. Withdrawal symptoms associated with discontinuing stimulant use include fatigue, depression, and disturbance of sleep patterns. Repeated use of some stimulants over a short period or high doses can lead to feelings of hostility or paranoia. Further, taking high doses of a stimulant may result in a dangerously high body temperature and an irregular heartbeat. There is also the potential for cardiovascular failure or lethal seizures.

Intravenous amphetamine produces euphoria, similar to but more sustained than that following the use of cocaine. As abuse of prescription amphetamines was recognized in the 1960s and 1970s, physicians prescribed less of the drugs for medical conditions such as depression and obesity. Clandestine laboratories manufacturing amphetamine emerged and continued to be active into the 2000s. Their preferred substance is methamphetamine, which can be synthesized easily. Since intravenous use of methamphetamine is usual, and tolerance quickly occurs, larger and more frequent doses become required to achieve the desired effect. Toxic effects supervene, with repetitive face and hand movements and stereotyped behavior; for example, the user assembling and dismantling mechanical objects. A full-blown paranoid type of psychosis may develop, with loss of reality and delusions of persecution. Individual susceptibility to these toxic effects varies greatly. Polydrug abuse of amphetamines is common; coadministration of amphetamine with heroin (speedball) or a barbiturate is believed to optimize the pleasurable effects while minimizing the toxic ones.

The most common indication for the prescription of stimulants is ADHD, and prescription drug treatment for this condition has been steadily increasing over the past years, especially in adolescents and college students. Newer preparations have emphasized delayed-release mechanisms and other methods of lengthening the duration of therapeutic serum drug levels in attempts to overcome the limitations of those stimulants with short-half lives. Of all prescription medications, methylphenidate has the highest prevalence of nonmedical use among adolescence. Misuse of prescription stimulants typically involves short-acting formulations. In August 2006, the FDA called for new warnings on stimulants used for ADHD. Treatment of addiction to prescription stimulants, such as methylphenidate, is often based on behavioral therapies that have proven effective in treating cocaine and methamphetamine addiction. Overdose is frequently cited as a reason for stimulant-related emergency department visits. Antidepressants may enhance the effects of a stimulant, and stimulants in combination with over-the-counter cold medicines containing decongestants may cause blood pressure to become dangerously high or lead to irregular heart rhythms. Therapeutic doses are lower than doses that are abused. For example, the doses of methylphenidate used for attention deficit disorder are typically below the level expected to produce reinforcement. However, higher doses and intravenous use can result in a rapid development of dependence.

Appetite suppressants cover a range of compounds, from the decongestant phenylpropanolamine (often available without prescription), to powerful amphetamine analogues (chemical variants). Most are stimulants, although one, fenfluramine, is quite sedative. As with the amphetamines, patterns of use and abuse vary a great deal, from chronic daily ingestion of a therapeutic dose to binge or spree use of large quantities. The appetite suppressants that act as amphetamines are more likely to be abused. Withdrawal symptoms include tiredness, dysphoria (emotional discomfort), and depression. In the early to mid-1990s, two prescription diet drugs, fenfluramine (often taken with phentermine and popularly known as fen-phen) and dexfenfluramine (Redux) grew in popularity. These drugs stimulated production of the brain chemical serotonin, creating a feeling of satiety. In 1997, reports of heart valve disease in women taking fen-phen or Redux began to surface. By September 1997, the drugs dexfenfluramine and fenfluramine were withdrawn from the U.S. market by their manufacturer, American Home Products. Phentermine (Fastin, Adipex, Ionamin) remains available in the market as its use alone has not been associated with the adverse health effects of the fenfluramine-phentermine combination.

EPIDEMIOLOGY AND TRENDS

Prescription drug abuse is widespread in the general population, and research in the 2000s has

focused on ascertaining its prevalence and correlates, including common comorbid psychiatric disorders. Historical evaluation of prescription drug abuse has been limited by the inconsistent definition of abuse and dependence, lack of drug-specific data, and lack of data on comorbid conditions, The prevalence of nonmedical use of prescription drugs remains highest for opioids and amphetamines; these two drug categories are also associated with the highest rates of abuse and dependence in the general population. Rates of prescription drug abuse and dependence tend to be higher among men than women. In addition, prescription drug abuse and dependence frequently begins with stimulant abuse and during adolescence. Numerous epidemiologic surveys have also found consistent associations of such abuse with alcohol use disorders, as well as mood, anxiety, and personality disorders. Thus, treatment of prescription drug abuse may require a comprehensive psychiatric assessment, including the evaluation of comorbid substance use and psychiatric disorders. Research has also demonstrated that abuse of prescription drugs is highly disabling but frequently remains untreated, despite highly effective and available treatment options.

Several factors may be contributing to the availability of prescription drugs that may result in abuse. The most common methods of diversion of controlled prescription drugs include: (1) "doctor shopping" (an individual visits several physicians who write a prescription for a controlled substance, which the individual then fills at different pharmacies), (2) illegal online pharmacies, (3) purchasing from drug dealers, (4) receiving from friends and family, (5) and negligent/intentional overprescribing by physicians or other practitioners. Prescription drug manufacturers have taken steps to minimize the potential harms of prescription drug abuse. National plans for addressing the rising prevalence of prescription drug abuse includes the establishment of a national All Schedule Prescription Electronic Reporting Program, a nationwide registry of all substances prescribed for an individual. In addition, the federal government has set up the Drug Abuse Warning Network (DAWN), which collects data on drug-related crises from several hundred hospital emergency rooms in metropolitan areas around the country.

See also **Iatrogenic Addiction; Obesity.**

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PRESCRIPTION DRUG MONITORING PROGRAM.

In the fiscal year (FY) 2002, the U.S. Congress appropriated funds to support the Prescription Drug Monitoring Program (PDMP) as a part of the U.S. Department of Justice Appropriations Act (Public Law 107–77). According to the Department of Justice, PDMPs are designed to help states prevent or detect the diversion and abuse of controlled pharmaceuticals at the retail level. These programs can easily collect and analyze prescription data using a state-level data collection and analysis system, thus enhancing the ability to use this data and facilitating the exchange of data between states.

To receive funding and implement the program, states or territories must have legislation or regulations in place or pending that require the submission of dispensing data to a centralized database and authorize or designate a state agency to implement and administer the program. Planning grants and enhancement grants are also available. Technical assistance in the development of this legislation is provided by the Prescription Drug Monitoring Project of the National Alliance for Model State Drug Laws (NAMSDL). NAMSDL provides access to model state laws and policy resources for planning, implementing, or enhancing PDMPs. These efforts include maintaining a listserv, monitoring legislation and regulatory changes, and distributing bimonthly PDMP updates.

As of November 2007, 20 states had implemented such programs and 23 states were in the implementation process, which excludes Arkansas, Delaware, Georgia, Maryland, Nebraska, South Dakota, and Wisconsin. Maryland introduced legislation during the 2008 session, but it did not pass. In an evaluation of state PDMPs conducted by Simeone Associates in 2006, researchers assessed both indirect and direct routes that may be used by these programs to decrease (regulate prescribing behavior) or hold steady (regulate dispensing behavior) the supply of controlled pharmaceuticals and thus decrease their abuse. They found that PDMPs that included Schedule II pain relievers and stimulants reduced the per capita supply of these drugs, which, in turn, reduced the probability of their abuse. In addition, states that were proactive in their use of a PDMP were more effective than those that were reactive.

COMPONENTS AND DATA ELEMENTS

Although all states and territories must apply for funding using the same process, the type of PDMP and the drugs covered can vary from Schedule II to Schedule V. PDMPs may be either reactive or proactive, which means that they can be used to generate reports in response to specific inquiries or to conduct investigations that generate unsolicited reports whenever suspicious behavior is detected.

The NAMSDL identified seven components for a strong prescription monitoring statute/program, which are listed below and described on its Web site.

1. Drugs monitored should include all state and federally controlled substances and other drugs

of concern documented to demonstrate a potential for abuse by law enforcement and addiction treatment professionals.

2. The monitoring system should proactively provide information to law enforcement and occupational licensing officials to support prescription drug-related investigation. Information without identifying information should also be provided to researchers, policymakers, and educators to support research, prevention, and other efforts.
3. The system should enable specific individuals, such as dispensers, physicians and other prescribers, law enforcement, and occupational licensing officials, to request specific information.
4. Individuals receiving information from the system should demonstrate that they know how to responsibly and properly use it.
5. An evaluation should be conducted to identify cost benefits and recommended improvements.
6. Statutory provisions should include confidentiality protections to prevent the improper use of the system or the information received from it.
7. Statutory provisions, regulations, or interstate agreements should be implemented to prevent interstate misuse and abuse of prescription drugs.

The data elements most commonly found in PDMPs are: name/ID and/or address of practitioner/dispenser/pharmacy; practitioner's/prescriber's and/or dispenser's DEA registration number; date prescription/medication filled or dispensed; name/address for the patient/recipient; patient's/recipient's data of birth; national drug code number of the controlled substance dispensed; and the quantity of the controlled substance prescribed or dispensed. All of these items are captured by the PDMPs of ten or more states. Other, rarer items collected include: the pharmacy number, prescription number, prescription form number, patient's/recipient's ID number, and the dosage or strength of the controlled substance prescribed.

OTHER USES FOR PRESCRIPTION DRUG MONITORING PROGRAMS

PDMPs can be used to track specific types of drugs or activities. For instance, 13 of the 20 states operating PDMPs as of 2008 require out-of-state mail-order pharmacies delivering or dispensing drugs into their states to enter data into the PDMP. Three states do not require this participation, and the remaining four lack the laws necessary to require the participation of mail-order pharmacies. Other innovations include a Web portal implemented by the Maine PDMP to increase users' ability to input and access the data. Texas has used data from its PDMP to support investigations into *pill mills*. And, licensure boards and law enforcement in Kentucky use data from their PDMP to produce geographic information system (GIS) maps that identify locations of controlled substance use by geographic area and increases and decreases in use over time.

Other types of electronic monitoring systems have also been developed or were pending as of 2008 such as pseudoephedrine monitoring systems and Department of Health and Human Services (DHHS) drug monitoring systems. The National All Schedules Prescription Electronic Reporting Act of 2005 requires that the DHHS award grants to establish or improve electronic drug monitoring programs. However, as of 2008, no funds had been appropriated for this effort, and it remained unclear how this act would relate to the original PDMPs. During FY2008, some states began to develop electronic tracking systems to monitor compliance with existing restrictions on the sale and purchase of pseudoephedrine products. NAMSDL was working with these states to ensure that these systems are interoperable with other systems such as PDMP.

See also **Prescription Drug Abuse; U. S. Government Agencies.**

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PREVENTION. Prevention of substance abuse is generally defined as either *demand reduction* through education and behavior change strategies to reduce precursor risk factors or to increase protective

factors; or *supply reduction* through increasing taxes and penalties, better enforcement, and interdiction. However, in some countries, prevention also includes *harm reduction approaches*, such as designated drivers, overdose prevention hotlines, checking drugs at raves, and providing clean needles. *Primary prevention* approaches are used before individuals begin regular use, *secondary prevention* approaches reduce use through screening and early intervention, and *tertiary prevention* approaches include treatments to stop drug use and associated problems. In 1995 the area of *primary* prevention was further divided by the Institute of Medicine (IOM) into three types: (a) *universal prevention* targeting low-risk general populations (e.g., students, families, or communities through media campaigns); (b) *selective prevention* targeting at-risk groups of individuals (e.g., children of substance abusers or prisoners or Native American children); and (c) *indicated prevention* targeting those with identified or diagnosed precursors of alcohol or drug abuse such as aggression, conduct disorders, thrill-seeking, or delinquency.

The length or dosage (number of contact hours) of these prevention approaches differs for each of these three primary prevention types. Namely, indicated primary prevention programs are generally longer and address more risk and protective factors than do those for general populations of low-risk youth in schools. Programs conducted for all youth or families in a school or community are universal prevention programs and are generally shorter in number of sessions and time per session than selective or indicated programs.

Sometimes indicated prevention approaches identify and prevent greater drug use in individuals who are experiencing early signs of substance use; technically, this should be defined as secondary prevention. Recently the White House Office of National Drug Control Policy (ONDCP) began stressing secondary prevention approaches in its Demand Reduction Themes because non-dependent users do not perceive the negative consequences of drug use and introduce friends to drugs. This type of secondary prevention will require effective early identification and intervention programs by school, workplace, social service, justice, and primary healthcare settings. In February 2008 the president released the 2008 National Drug Control Strategy of the White House ONDCP, its goals being to reduce drug use in America by stopping use before it starts, healing America's drug users, and disrupting the market for illegal drugs (ONDCP, 2008).

PREVENTION APPROACHES

Prevention of substance abuse is now a sophisticated science. It has moved beyond less effective approaches of the 1970s and 1980s that included scare tactics, one-time drug-prevention assemblies, and "Just Say No" campaigns. Because taxpayers and state and federal agencies require accountability, prevention practitioners are using a wide variety of evidence-based prevention programs to match the needs of different participants. Lists of programs that have been studied for effectiveness can be found at these websites: the National Institute of Drug Abuse (NIDA, http://www.nida.nih.gov/), the Substance Abuse and Mental Health Administration (SAMHSA) Model Programs list (http://www.modelprograms.samhsa.gov), the White House Helping America's Youth guide (http://guide.helpingamericasyouth.gov), the Office of Juvenile Justice and Delinquency Prevention's (OJJDP) Strengthening America's Families at the University of Utah (http://www.strengtheningfamilies.org), or BluePrints at the University of Colorado (http://www.colorado.edu/cspv/blueprints/model/overview.html).

A number of these evidence-based programs, especially comprehensive ones targeting the family and community, also reduce other behavioral problems such as delinquency, family violence, child abuse, teenage pregnancy, and school failure. Hence, investment in these programs can have additional positive effects.

COST BENEFITS

Most research-based prevention programs are cost beneficial. For each dollar spent, they save at least $4 in costs for drug abuse treatment and counseling. Considering other costs to society, such as crime, unemployment, and health costs, the cost effectiveness of good drug abuse prevention is even greater. Aos and associates' (2004) analysis showed positive cost/benefit ratios ranging from $102.29 saved for every dollar spent for the *Minnesota Smoking Prevention Program* to a low of $3.43 for the *All Stars Program*. Only two programs produced losses—*D.A.R.E.* and *S.T.A.Rs for Families*. Not all substance abuse prevention programs

are listed in this category, since some fall into the Youth Development section, such as the *Seattle Social Development Project* ($3.14/$1 spent), *Guiding Good Choices* ($11.07/$1 spent), and the *Strengthening Families Program for Youth 10–14 Years* ($7.82/$1 spent), which were developed and tested for drug use prevention. The highest cost-benefit ratios of all educational and social services programs are for substance abuse prevention programs. Their ratios are much higher than Preschool Education Programs (highest was $2.34/$1), Child Welfare/Home Visitation Programs (highest was $2.88/$1 for the *Nurse Home Visitation Program*), Teen Pregnancy Prevention Programs, or many Juvenile Offender Programs. Some had spectacularly negative results. For example, the *Scared Straight* program cost $54 per youth but resulted in increased costs of over $11,000 per offender. Not all prevention programs work, so states and agencies should invest in programs that studies show to have a high level of effectiveness.

SELECTING THE BEST PREVENTION APPROACHES

Because there is not one best program, practitioners should conduct a needs assessment of their target population first. They should determine the most salient risk or protective factors and then select the best prevention approaches to address those needs. The Center for Substance Abuse Prevention (CSAP) recommends standardized needs assessment instruments for states to determine how to best use their Block Grant funds for prevention. A number of communities and states also use the *Communities That Care* (Hawkins & Catalano, 1999) student needs assessment survey and matching system to select evidence-based prevention programs.

A number of factors should go into selecting the best program for a local population: age of children, ethnicity and language, length of program, cost, staff required, outcomes improved, and level of clients' dysfunction (e.g., low-risk universal families, selective high-risk families, or indicated in-crisis families). In addition, Web sites or reports that include meta-analyses enable practitioners to pick the most effective program for their investment. Factors to consider are the quality of the research, the amount of research, and the replication of program by independent researchers (Flay et al., 2005). After narrowing the search to two or three programs, focus groups of parents or staff can review the materials. Other considerations include the availability of training, technical assistance, and evaluation services as well as the costs.

PRINCIPLES OF EFFECTIVE PREVENTION PROGRAMS

Characteristics of effective prevention programs, called *principles of prevention*, can be used to judge the potential effectiveness of different programs. Both NIDA and ONDCP have published lists of principles for substance abuse prevention programs. Nation and colleagues (2003) used a "review of reviews" approach to extract effectiveness principles from research articles on prevention programs in four content areas—substance abuse, risky sexual behavior, school failure, and juvenile delinquency and violence. Nine program characteristics were consistently associated with effective prevention programs: theory-driven, comprehensive, appropriately-timed, socio-culturally relevant, sufficient dosage, varied teaching methods, positive relationships, well-trained staff, and outcome evaluation.

WHAT WORKS IN PREVENTION PROGRAMS

What works in prevention, according to ONDCP, are approaches that are primarily punitive: drug testing in schools and workplaces, community coalitions with *supply reduction* strategies (e.g., increasing taxes, using restrictive zoning, increasing sting operations, and passing local regulations to restrict outlet licenses), drug courts, threats to remove children from drug-using parents, brief screening interventions, and referrals to treatment (ONDCP, 2008). Few randomized control trials of these environmental approaches exist to prove these approaches work. No mention is made of positive youth development or family programs, although prevention researchers, expert review committees of federal departments (NIDA, NIAAA, SAMHSA's NREPP, CDC), and expert review groups (e.g., the Cochrane Collaboration Reviews in Medicine and Public Health at Oxford University) found these primary *demand reduction* approaches effective.

Most research on preventing alcohol and drug abuse has focused on junior-high-school-aged students, because most individuals initiate substance use during this time. Less is known about other developmental periods; however, this entry

discusses what is known about the most effective approaches for both children and adolescents.

To increase accountability and positive outcomes, substance abuse funding agencies are increasingly requiring that funding be used only or primarily for evidence-based programs (EBPs). Best practices are those with research evidence showing decreased substance use, delayed age of use onset, improved protective factors, and decreased risk factors related to later use. Research literature contains many evidence-based programs (EBPs) with sufficient effectiveness as tested in large-scale, randomized, controlled intervention trials to warrant dissemination and adoption by schools and communities. Effective EBP prevention approaches have been identified by federal review committees and are listed on the Web sites of federal agencies. Syntheses of best practices in evidence-based prevention practices have been published by the Institute of Medicine (IOM, 1995), CSAP (1998), NIDA *Preventing Drug Use Among Children and Adolescents* (NIDA, 2008), and researchers (Hawkins & Catalano, 1999; Kumpfer & Alder, 2003).

Different approaches generally included in a comprehensive prevention plan are family-focused approaches, child-only approaches, and community- or school-change approaches. These are briefly reviewed below in order of effectiveness according to meta-analyses of amount of positive change.

Parenting and Family Focused Approaches. Strong families are key to preventing adolescent drug use problems. For instance, youth report on the PRIDE survey (2006) that parent disapproval is the major reason *not* to use drugs. Also almost three-fourths of parents believe they are the most effective deterrent. However, they fail at monitoring youth behaviors and dramatically underestimate the percentage of youth using alcohol versus the percentage actually reporting use (11% versus 42%) (PRIDE, 2006). The general logic of a family-focused approach is that by teaching parents to be better parents, improving their parent/child relationships, and increasing effective discipline and monitoring, children will have better developmental outcomes in all areas, including tobacco, alcohol, and drug use. Family programs appear to be the most effective prevention programs for many adolescent problems.

Several attempts have been made to classify the different types of family-focused approaches for prevention. Researchers in this area disagree, however, about definitions of family-focused approaches. The CSAP Prevention Enhancement Protocols System (PEPS, 1998) review of family-focused approaches defined eight approaches, but found only four approaches with sufficient research evidence to prove they worked for substance abuse prevention: (a) behavioral parent training, (b) family skills training, (c) family therapy, and (d) in-home family case management or support programs. Since this 1998 CSAP review, the low-cost *Family Matters* program of involving parents in substance-abuse-prevention homework assignments with their children is showing promise as a cost effective approach (Bauman et al., 2001).

Kaminski and associates (2008) at the Centers for Disease Control (CDC) have analyzed the critical core components of EBP family interventions from 77 studies of programs for 0–7-year-olds. Because the presence of conduct disorders in early life often precedes later delinquent, aggressive, and risky behaviors in adolescence, they reasoned that effective parenting could reverse this trend. The *core components* of effective parenting and family interventions include:

1. Practice time for parents to interact with their children while therapists or group leaders are available for coaching.
2. Teaching parents to interact positively with children (e.g., showing enthusiasm and attention for good behavior and letting children take the lead in play activities).
3. Increasing parental attention and praise for children's positive behaviors, explaining children's normal development to promote realistic expectations for children's behaviors, improving family communication (e.g., increasing active listening and reducing criticism and sarcasm), and teaching effective and consistent discipline (e.g., time-outs).
4. Teaching children social skills, so they get along better with parents, peers, and teachers.
5. Assigning and encouraging home practice assignments to improve generalization of new behaviors at home.

(For additional reviews of effective family-strengthening approaches, see Kumpfer & Alvarado

[2003] and the OJJDP Strengthening America's Families Web site).

A national review of family-strengthening approaches conducted in 2000 found about 35 evidence-based practices (Kumpfer & Alvarado, 2003). However, only 14 family programs have been tested in randomized control trials, and only seven were independently replicated, thus meeting the criteria for the highest level of evidence of effectiveness, Exemplary I Programs. The Exemplary I family programs for ages 0–5 include *Helping the Noncompliant Child* and *The Incredible Years*. The only Exemplary I program for ages 6–12 is Kumpfer's *Strengthening Families Program*. The only pre-teen and adolescent programs included in this category are *Functional Family Therapy*, *Multisystemic Family Therapy*, *Preparing for the Drug Free Years* (now called *Guiding Good Choices)*, and *Treatment Foster Care*. According to the Cochrane Collaboration Reviews in Medicine and Public Health meta-analysis of all school-based universal alcohol-prevention programs, the *Strengthening Families Program for 10–14 Year Olds* is twice as effective as the next best program, *Preparing for the Drug-Free Years* (Foxcroft et al., 2003).

Overall, family-focused approaches averaged effect sizes (as measured by Cohen's d and measuring amount of change) were nine times larger than child-only prevention approaches (d = 0.96 ES versus d = 0.10ES) as shown in Table 1 below (Kumpfer, Alvarado, & Whiteside, 2003). Effect sizes measure the amount of change in the treatment group compared to the control group. A d effect size of 1 is about equivalent to one standard deviation of change or a large change. A small change is under d=.20. In selecting the best family-focused program, the prevention practitioner must consider the target population's need for a universal, selective, or indicated prevention program as well as the age of the child, ethnicity, and special needs. A matrix of these programs by prevention level and age is available on the Strengthening America's Families Web site (http://www.strengtheningfamilies.org) along with program descriptions and links to the program developer's Web sites.

The United Nations Office of Drugs and Crime has developed with Kumpfer an updated search for evidence-based parenting and family programs worldwide and identified 185 noteworthy programs. A protocol with steps for culturally adapting these EBPs can be found on their Web site (http://www.unodc.org/) along with a publication by Kumpfer and associates (2008) on steps for local and cultural adaptations.

School-based affective	−.05
Knowledge plus affective	.05
Life or social skills training	.28
Average ES youth-only programs	**.10 ES**
Parent skills training	.31
Family therapy	.45
Family skills training	.82
In-home family support	1.62
Average ES family interventions	**.96 ES**

Table 1. Average effect sizes of youth-only and family prevention interventions for substance abuse prevention. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Youth-only Prevention Approaches. The most rigorously tested and effective approaches include social skills and life skills training programs, which are implemented in many settings (e.g., schools, community centers, churches, and youth clubs). Other child-only school or community agency approaches for reducing substance abuse include mentoring, tutoring, and providing alternative activities, recreation and leisure programs, wilderness challenge programs, and community service programs. However, little research has been done on these programs. Additionally the most well-researched mentoring program, *Big Brothers/Big Sisters*, costs about the same as its benefits—a $1.01 benefit per $1.00 spent (Aos et al., 2004). School-based programs are most successful in reducing tobacco use, followed by drug use, and then alcohol use.

Critical core components of effective school-based programs include involvement with positive role models or mentors, sufficient number of contact hours, interactive/cooperative learning, and booster sessions. Interventions run by mental health clinicians are two to three times more effective than programs implemented by peers, teachers, police officers, or others (Tobler et al., 2000). The effect size (ES) in reducing substance use varies considerably by type of child-only approach.

Life Skills Training Programs have the highest positive results as measured by average effect size or amount of change. These Life Skills programs include refusal skills, life skills (e.g., communication, problem-solving, coping, social/dating, goal-setting, stress management, and media literacy), and public commitments not to use. The average effect size for these child-only programs (N=206) was 0.10, which is quite small; however, the most effective programs were Botvin's *Life Skills Training* (LST) (Botvin, 1995) and Schinke's and associates (2000) *Smart Moves for Native Americans*, which had higher effect sizes averaging 0.28. One of the first to study the use of computer technology in substance abuse prevention, Schinke and associates (2004) tested a 10-session computer-based (CD-ROM) version of his life skills program with and without parental involvement (30-minute video tape and two newsletters on effective parenting). They found that parental involvement improved the outcomes for alcohol use, but both versions were more effective for drug and tobacco use reductions compared to a no-treatment control.

The least effective program, which produced slight negative effects, was the combination of *Knowledge-only* and *Affective Education* programs that were popular in the early 1980s. The widely promoted *D.A.R.E.* program (a social skills program based on the effective SMART program) failed to prevent drug use (Harrington et al., 2000). One possible reason for the failure of *D.A.R.E.* is that police officers tend to lecture and tell stories. Prevention programs using interactive, skills training methods to change behaviors as opposed to didactic lecture methods to change knowledge are more effective, particularly for minority youth. A new version of *D.A.R.E.* is being developed and tested by Sloboda. However, the initial cost-benefit ratio for *D.A.R.E.* is estimated at a net loss of $99 per student (Aos et al., 2004), because there are minimal positive outcomes (d = 0.03 or very small) (Tobler et al., 2000).

Community Coalition or Environmental Change. Community coalition approaches are currently popular with the federal government. Most funding for community prevention grants provided by ONDCP and SAMHSA CSAP goes for the Anti-drug Communities Support Program, which funds 750 coalitions for about 90 million total. In 2008 they funded about 150 new community coalitions at $125,000 each. However, the United States has about 4,000 drug prevention coalitions. These coalitions typically follow a comprehensive community approach that changes the total community climate and norms. They can only spend 20 percent of their federal budget to implement multiple prevention strategies, including individual, school, workplace, and family prevention approaches. The bulk of the funding is used for advocacy, media campaigns, meetings, and environmental policy change.

Examples of evidence-based community partnership or coalition approaches include the *Midwestern Prevention Program*, *Project Northland*, and the *Communities That Care (CTC)* model (Hawkins & Catalano, 1999). Research on *Communities That Care* is being conducted on 41 matched communities in seven participating states (Hawkins, Catalano, & Arthur, 2000). This project tracks the history of risk- and protection-focused prevention planning and assesses the effectiveness of the CTC coalition model in reducing risk factors, increasing protective factors, and decreasing youth substance abuse. The CTC community coalition model is based on six phases: (a) needs assessment using standardized CTC school and community leaders surveys, (b) prioritization of risk and protective factors for intervention, (c) selection of tested interventions to address needs, (d) implementation of science-based prevention interventions, (e) monitoring of changes in targeted risk and protective factors, and (f) adjustment of interventions as indicated by performance data.

Evaluations found that community coalitions were effective if they were organized in areas with a high degree of community readiness, progressed from planning to implementation within the first two years, implemented proven prevention strategies, and had strong, empowering leaders who promoted a shared vision, utilized members' talents, and avoided or resolved conflict (Yin & Ware, 2000). An analysis of 10 percent of the more than 250 CSAP-funded community coalitions found community coalitions were effective in reducing alcohol and drug abuse in eighth and tenth grade boys and adult males as compared to matched communities without coalitions. Community coalitions were not effective for girls or women and, in fact, resulted in increases in drug use in eighth grade girls (Yin et al., 1997). Because coalitions typically focus on implementing environmental

policies, such as access to tobacco and alcohol, they often do not include funding for school- and family-strengthening approaches, which have more impact on reducing drug abuse in girls.

Policy Change Strategies. Community coalitions generally are most effective in changing community policies and laws related to age of legal purchase, cost of tobacco or alcohol, availability of products, density of outlets, keg registration, server training, counter-advertising, legislating warning labels, and other environmental changes. Many alcohol-misuse interventions are implemented through an overall community coalition mobilization. Some examples of effective alcohol-prevention coalitions include the *Community Trials Project*, *Saving Lives*, and *Project Northland*.

Because states have less funding for substance abuse prevention services, they turn to policy change strategies, which cost less and can generate increased tax dollars. Despite a recent upswing in the popularity of policy approaches, only a few policy approaches, such as increasing the age of purchase and boosting taxes and cost of tobacco or alcohol, are effective in reducing substance use (Wagenaar & Toomey, 2002). Sting operations to reduce sales of tobacco or alcohol have not reduced adolescent use, although they are effective in reducing sales to minors. Sting operations staffed by coalition youth along with increased enforcement and limiting licenses resulted in a reduction in sales to minors of about 50 percent to 20 percent between 1997 and 2000. However, during that time tobacco use did not decrease in minors. Teens get adults to purchase for them or steal cigarettes.

The effects of community-based alcohol prevention are modest, even though great effort and funds have been expended on them. Cost-benefit studies are needed to help communities understand how much improvement they can expect. Increasing the cost of alcohol and increasing the legal drinking age or maintaining it at 21 years appears to be an effective approach to reducing consumption among youth.

COLLEGE AGED YOUTH PREVENTION

Despite documented risks, few prevention strategies aimed at college-age drinking have been successful (NIAAA, 2000). The Department of Education's Fund for the Improvement of Postsecondary Education (FIPSE) was successful in funding drug prevention centers on college campuses nationwide. Many colleges continued these prevention centers when the seed funding ended. Primary prevention approaches adopted in colleges are media campaigns, alcohol and drug policy revisions, early identification, and referrals to counseling. Changing the perception that most college students are substance users through published needs assessment surveys is also effective.

Little research exists on prevention strategies that work for college students. The NIAAA Task Force in 2002 suggested that generalized strategies effective with adults should work (e.g., increasing taxes and cost of alcohol, increasing enforcement and consequences of violating minimum legal drinking age laws and driving under the influence, and instituting policies and training for servers of alcoholic beverages). Strategies recommended specifically for college/university students include normative education and stress/coping strategies as well as correcting false beliefs about the effects of alcohol and increasing motivation to reduce drinking. Combining approaches into a comprehensive campus-wide approach should be more effective. More information on the NIAAA Task Force's report can be found on their website.

COCHRANE COLLABORATION REVIEWS

The World Health Organization Cochrane Collaboration Reviews in Medicine and Public Health has conducted several meta-analyses of substance abuse prevention programs. One of the first was of school-based alcohol prevention (Foxcroft et al., 2003). Of 56 studies, 20 had no or negative results. They concluded that the *Strengthening Families Program 10 to 14 Years* (Kumpfer, Molgaard, & Spoth, 1996) was twice as effective for preventing alcohol use after at least a two-year follow-up. The next best program was also a parenting program, *Preparing for the Drug-free Years* (PFDY). The next most effective programs were Schinke's (2000) *Smart Moves for Native Americans* and Botvin's (1995) *Life Skills Training* (LST). A 2006 meta-analysis of drug abuse prevention also found SFP to be one of only two promising programs, the other being a social marketing media approach (Gates et al., 2006). BluePrint program reviewers found positive results in evidence-based programs depend heavily on fidelity

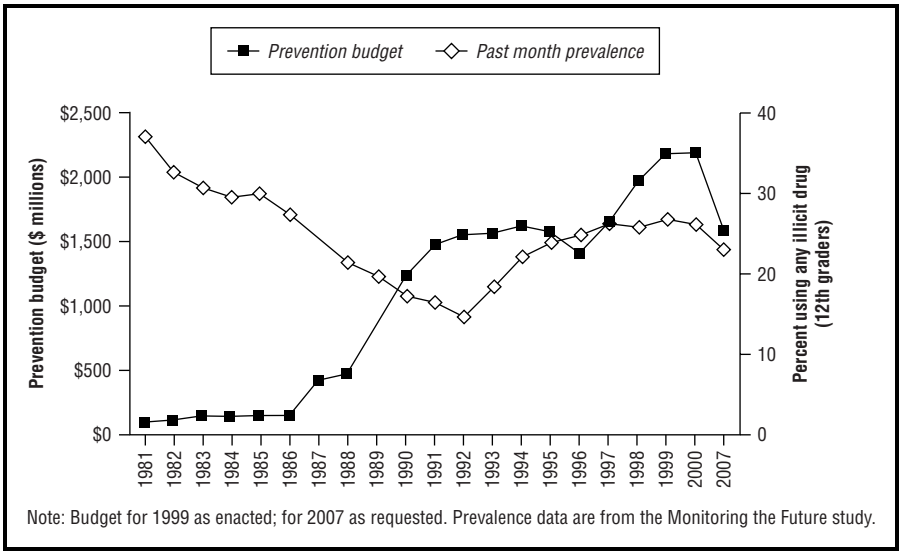

Figure 1. Prevention budget and prevalence of drug use among 12th graders, 1971–2007. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING.

to the original model and high quality implementation (Elliott & Mahalic, 2004).

FUNDING FOR PREVENTION AND TREATMENT

Funding for drug treatment and prevention has not kept pace with the need. Despite increased recognition of the cost effectiveness of prevention programs, Dr. Sloboda, President of the Society for Prevention Research, noted funding difficulties (Sloboda, 2008). She said in her presidential address at SPR, "In a squeeze, budgets for prevention have been easy targets for cash-strapped governments. In the U.S., prevention funding had already been *cut by up to 25 percent* when investments in interdiction that are not working have increased. Investments to support the Safe and Drug-Free Schools and Communities Act, for example, fell from $346 million in 2001 to $270 million last year."

According to ONDCP, the percentage of the total federal budget for prevention was 12 percent in 2008, compared to 14 percent in 2000. The National Drug Control Budget rose 57 percent from $12.2 billion to $19.2 billion between 1994 and 2001, but dropped to 12.9 billion in 2007. During the rise from 1994 to 2001, prevention and treatment funding increased only 33 percent and 44 percent respectively, while international efforts increased 175 percent, interdiction efforts increased by 68 percent, and domestic law enforcement by more than 60 percent. Without increased funding for drug prevention and treatment, it is difficult to reduce the demand for drugs (see Figure 1).

Despite these increases in total federal funding over the last two decades, the "War on Drugs" has been criticized for its failure to reduce drug use or to produce a consistent and fair legal policy (Battin et al., 2007). Overall, about 90 percent of U.S. funding for the War on Drugs goes for supply reduction, including funding for interdiction, crop eradication, and border patrols, and not for demand reduction or prevention. Despite this, adolescents report in the *Monitoring the Future* surveys that drugs are as available as in the late 1980s or early 1990s, depending on the drug (Johnston, O'Malley, Bachman, & Schulenberg, 2007). What emerges from this picture is an erosion of funding for prevention in America, which can only lead to increased substance use in the future. Citizens must become more vocal and involved in local and national substance abuse prevention policy making. They should promote increased prevention funding and support prevention programs that work to promote not just reductions in illegal drug use but also in many other associated social and health problems.

See also **Crime and Drugs; Gangs and Drugs; Prevention, Education and.**

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KAROL KUMPFER

PREVENTION, EDUCATION AND.

In its broadest sense, prevention refers to the reduction of the supply of drugs through law enforcement actions and the demand for drugs through public health and education programs. Prevention can occur throughout the life span and in five distinct domains: individual, family, peer, school, and community. Public health and education prevention programs reduce the demand for drugs by stopping use or abuse after it starts or providing people with the resources and support they need to avoid using them in the first place. Thus, such programs may be designed to reach individuals before they initiate use (primary prevention), provide screening and early intervention (secondary prevention), or prevent the progression of an existing drug problem (tertiary prevention). Successful programs help participants strengthen existing, and develop new, protective factors (e.g., strong neighborhood or familial attachments) while reversing or reducing modifiable risk factors (e.g., early aggressive behavior or lack of parental supervision) and can operate on three levels. Universal programs target a general population, selective programs target a subset of the general population known to be at risk, and indicated programs target individuals already experimenting with drugs. The higher the level of risk of the target population, the younger the participants should be when they initiate the program and the more intensive the program should be. Research has shown that successful programs are also developmentally appropriate and culturally sensitive.

In 1997 the National Institute on Drug Abuse (NIDA) produced a research-based guide to prevention programs for parents, educators, and community leaders that lists the principles of effective research-based prevention programs and provides guidance on thinking about, planning, selecting, and delivering community-based prevention programs. The second edition, released in October 2003, provided 16 principles derived from NIDA-funded research on the origins of drug-abuse behaviors and effective prevention programs:

1. Prevention programs should enhance protective factors and reverse or reduce risk factors.
2. Prevention programs should address all forms of drug abuse, alone or in combination.
3. Prevention programs should address the type of drug-abuse problem in the local community, target modifiable risk factors, and strengthen identified protective factors.
4. Prevention programs should be tailored to address risks specific to population or audience characteristics, such as age, gender, and ethnicity, to improve program effectiveness.
5. Family-based prevention programs should enhance family bonding and relationships and include parenting skills; practice in developing, discussing, and enforcing family policies on substance abuse; and training in drug education and information.
6. Prevention programs can be designed to intervene as early as preschool to address risk factors for drug abuse, such as aggressive behavior, poor social skills, and academic difficulties.

7. Prevention programs for elementary school children should target improving academic and social-emotional learning by building self-control, emotional awareness, and communication and social problem-solving skills.
8. Prevention programs for middle or junior high and high school students should increase academic and social competence by building study habits, communication skills, peer relationships, self-efficacy and assertiveness, drug resistance skills, antidrug attitudes, and personal commitments against drug abuse.
9. Prevention programs aimed at general populations at key transition points, such as the transition to middle school, can produce beneficial effects even among high-risk families and children. Such interventions do not single out risk populations and, therefore, reduce labeling and promote bonding to school and community.
10. Community prevention programs that combine two or more effective programs, such as family- and school-based programs, can be more effective than a single program alone.
11. Community prevention programs reaching populations in multiple settings—for example, schools, clubs, faith-based organizations, and the media—are most effective when they present consistent, communitywide messages in each setting.
12. When communities adapt programs to match their needs, community norms, or differing cultural requirements, they should retain core elements of the original research-based intervention including structure, content, and delivery.
13. Prevention programs should be long-term with repeated interventions (i.e., booster programs) to reinforce the original prevention goals. Research shows that the benefits from middle school prevention programs diminish without follow-up programs in high school.
14. Prevention programs should include teacher training on good classroom management practices, such as rewarding appropriate student behavior. Such techniques help to foster students' positive behavior, achievement, academic motivation, and school bonding.
15. Prevention programs are most effective when they employ interactive techniques, such as peer discussion groups and parent role-playing, that allow for active involvement in learning about drug abuse and reinforcing skills.
16. Research-based prevention programs can be cost-effective. Similar to earlier research, recent research shows that for each dollar invested in prevention, a savings of up to $10 in treatment for alcohol or other substance abuse may be seen.

NATIONAL APPROACH TO PREVENTION: CENTER FOR SUBSTANCE ABUSE PREVENTION

The Substance Abuse and Mental Health Services Administration's (SAMHSA) Center for Substance Abuse Prevention (CSAP) works with states and local communities to develop comprehensive prevention systems that promote communities with healthy, drug- and crime-free environments at work and in school, supportive neighborhoods, and connections with families and friends. To further this mission, CSAP has developed a strategic prevention framework and a registry of proven and promising programs. It maintains four funding streams to support state and local efforts to implement the framework and programs.

Strategic Prevention Framework. The Strategic Prevention Framework (SPF) is a five-step data-driven strategic planning and community development process. It promotes youth development and builds assets and resilience while reducing risk-taking and other problem behaviors across the life span. In this way, CSAP ensures that implemented prevention programs are grounded in evidence-based research and that the outcomes of those programs are regularly monitored.

The five steps in the SPF are assessment, capacity building, planning, implementation, and evaluation. Assessment uses data to define and quantify substance use and its consequences. It enables states and communities to prioritize substance-abuse problems to determine how to focus future steps in the process. The second step is to build the capacity of the state or community to address these problems by engaging key stakeholders and mobilizing communities and resources. Once priority problems are identified and the state or community has the capacity to address them, the planning phase begins. Comprehensive

interventions are designed to impact specific risk and protective factors. Then the plans are implemented and evaluated.

The evaluation of a program should involve monitoring both the progress of the implementation and impact of the program over time. SAMHSA has identified 14 prevention measures in eight domains as a part of National Outcomes Measures (NOMs) to provide uniform measures for all federally funded programs. The domains are reduced morbidity, employment and education, crime and criminal justice, social connectedness, retention, access and capacity, use of evidence-based programs and strategies, and cost-effectiveness. Baseline reports on the NOMs for each state are based largely on national data sets, such as the National Survey on Drug Use and Health.

Sustainability and cultural competence make up the backbone of this process and are ongoing efforts throughout the process. Sustainability refers to the ability to maintain positive outcomes by making the SPF steps the norm and integrating them in the ongoing operations of state and local agencies. Sustainability is vital to ensuring that necessary resources (financial and otherwise) are secured to establish and maintain prevention values, processes, and partnerships over the long term. Cultural competence is the ability to communicate with participants from diverse geographic, ethnic, racial, cultural, economic, social, and linguistic backgrounds. Culturally competent programs are effective because they eliminate disparities between services and participants. They meet the needs of the people they serve.

Funding Mechanisms to Support Local Prevention Efforts. Currently CSAP maintains four grant programs to support states and communities implementing the SPF: The SPF State Incentive Grant (SIG), drug-free community grants, HIV grants, and methamphetamine grants. The SPF SIG is an infrastructure grant designed to support the implementation of the strategic prevention framework described above by states and federally recognized tribes and tribal organizations. The infrastructure provides a solid foundation for preventing the onset and reducing the progression of substance abuse and substance-abuse-related problems in communities. Thirty-seven SIGs were operating across the nation in 2008.

The cornerstone of the SPF SIG is the State Epidemiology Outcomes Workgroup (SEOW). The SEOW is responsible for completing the first step of the SPF by conducting both statewide and community level needs assessments. As of 2008, SEOWs were funded in all 50 states. The mission of the SEOW in Maryland, for instance, is to monitor the use of alcohol, tobacco, and other drugs and the consequences of their use in Maryland and its localities in order to identify and prioritize the prevention needs of the state and its local jurisdictions. To achieve this end, the Maryland SEOW will oversee the collection, interpretation, and dissemination of statewide and local data that quantify substance use and its consequences for Maryland. The reports prepared by the SEOW will be used to complete the remaining steps of the SPF process.

Drug-free community grants are a part of the Drug Free Communities Program that is run jointly by SAMHSA and the White House Office of National Drug Control Policy (ONDCP). In the most recent round of funding as of 2008, new grants were awarded to 90 communities and continuation grants were awarded to 646 communities in 49 states, the District of Columbia, Puerto Rico, and the Virgin Islands. These grants support community organizations that act as catalysts to increase citizen participation in substance prevention efforts directed at youth.

HIV grants were initially awarded in 2004. At that time, SAMHSA awarded more than $111 million to support states implementing the SPF to develop local capacity to address substance abuse by individuals (especially racial and ethnic minorities) living with and affected by HIV/AIDS. These funds have been used for mental health, treatment, prevention, outreach, training, and studying the costs associated with delivering integrated care. In FY2005, 25 states, the District of Columbia, and the Virgin Islands received funding to implement the SPF for substance-abuse and HIV/hepatitis prevention in targeted minority populations. In the most recent funding cycle, SAMHSA planned to support up to 46 cooperative agreements for community-based substance-abuse and HIV/AIDS prevention programs for at-risk racial or ethnic minority populations based on the SPF.

In response to increases in methamphetamine abuse across the country, SAMHSA awarded methamphetamine grants in FY2006 and FY2007. These grants were designed to support infrastructure

development and/or methamphetamine prevention interventions. The goal is to prevent, reduce, or delay the use of methamphetamine. Like the other SAMHSA/CSAP grants, this grant encourages the use of the SPF to build local capacity and implement evidence-based programs. Programs in eight states received awards in FY2006, and programs in Corona, California, and San Antonio, Texas, received grants in FY2007.

ASSESSMENT

The science of prevention has made great progress since the mid-1990s. Substance-abuse prevention programs have been shown to be cost-effective. Research-based estimates demonstrate that every dollar invested in prevention saves $10 in treatment and other expenses. SAMHSA/CSAP has established a strategic prevention framework with standards for evidence-based programs and measures to assess outcomes. The National Registry of Evidenced-Based Programs and Practices, for instance, includes 35 proven substance-abuse prevention and treatment programs and 92 legacy (effective or promising) programs to address co-occurring disorders, mental health, prevention, and treatment. The NOMs, described in an earlier section, ensure that the impacts of these programs are measured consistently and regularly. In spite of this continuing progress in understanding prevention and implementing effective programs, the George W. Bush administration's drug control budget continued to emphasize supply reduction programs over demand reduction programs. Funding for supply reduction programs increased 57 percent from FY2002 to FY2009, while funding for demand reduction programs grew by only 2.7 percent and prevention funding actually decreased 25 percent. This trend appears to be counter to current research and has made it increasingly difficult for federal, state, and local agencies to effectively implement the current prevention framework.

See also **Adolescents and Drug Use; Families and Drug Use; Homelessness, History of Association with Alcohol and Drugs; Models of Alcoholism and Drug Abuse; Parent Movement, The; Prevention.**

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E. ERIN ARTIGIANI

PREVENTION OF ALCOHOL RELATED HARM: THE TOTAL CONSUMPTION MODEL.

The total consumption model of alcohol is an important concept for anyone who wishes to understand the underpinnings of modern policy efforts to prevent heavy drinking and alcohol-related harm. The point of departure for this concept is a set of observations about how alcohol consumption is distributed in human societies and how the total, or mean, consumption per drinker is related to excessive drinking and alcohol-related harm.

The distribution of alcohol consumption in a population can be shown as a distribution curve in a diagram where the number of drinkers in a population is on the *y*-axis and the annual amount of alcohol intake is on the *x*-axis. This distribution curve could—a priori—take on different shapes. A popular assumption that normal drinkers and alcoholics (or "abnormal drinkers") constitute distinct categories of drinkers would imply that they are populations separated on the consumption scale and that the distribution of consumption occurs in two parts. If that were the case, the distribution of alcohol consumption

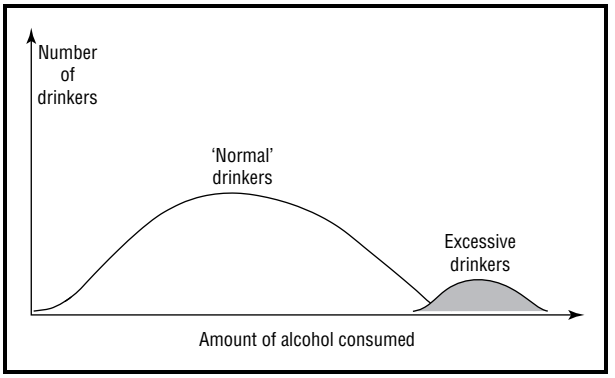

Figure 1. Hypothetical distribution curve of alcohol consumption. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

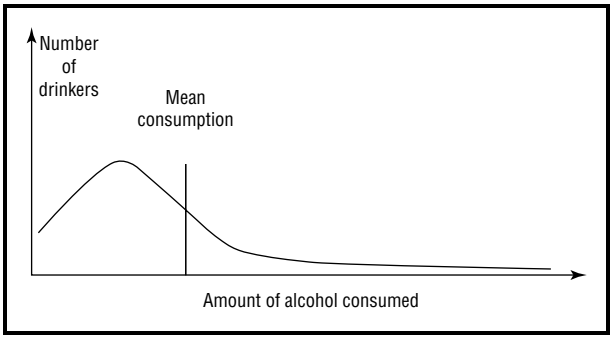

Figure 2. Example of empirical distribution of alcohol consumption. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

could take the shape illustrated in Figure 1. Starting on the left are the majority of normal drinkers, with a few people drinking very little in a year, then moving to an increasing number drinking greater amounts but less than the average amount, and finally, a declining number drinking more than the average amount, until the graph reaches the normal drinkers who drink much more than the average—and these are relatively few in number. In addition, there are a minority of "abnormal" drinkers; their drinking distribution also might be plotted as a bell-shaped curve, but this curve is shifted to the right of the distribution for normal drinkers. The two peaks in the distribution (one for normal and one for abnormal drinking) create a bi-modal distribution.

A large number of empirical studies in various populations have demonstrated, however, that the distribution of alcohol consumption does not resemble such a bi-modal distribution. The observed distributions in different populations with varying mean consumption do, in fact, display the same kind of distribution curve, which is *unimodal* (having one peak) and very skewed with a long tail toward high consumption levels. Such a skew distribution implies that the majority of drinkers consume less than the population average (see Figure 2). Moreover, this distribution implies that there is no clear separation between normal drinkers and excessive drinkers or alcoholics.

BACKGROUND

The relationship between total consumption (or mean consumption) and prevalence of excessive drinking was first noted by the French demographer Sully Ledermann (1956; 1964), and hence the model is also known as the Ledermann model. Ledermann's work on the distribution of alcohol consumption began in his earlier studies showing a significant co-variation in space and time between per capita alcohol consumption and mortality. This led to the assumption that the mean (per capita) alcohol consumption in a population is closely connected to the prevalence of excessive drinkers, who have an elevated risk of premature death. Ledermann proposed that the consumption distribution is a one-parameter lognormal distribution. A lognormal distribution means that the distribution is skewed with a long tail to the right and that, when plotted on a natural logarithmic consumption scale, the distribution is normal with a bell-shaped form. A one-parameter distribution means that there is constant relationship between the mean and the dispersion of the distribution; hence, it is also called a single-distribution model.

The critics of Ledermann have demonstrated, however, that the mathematical properties of the distribution of consumption are not as strict as he suggested (Bruun et al., 1975; Skog, 1985; Lemmens, 1991). For instance, the relationship between the mean and the dispersion of the distribution is not—as Ledermann suggested—constant, but varies to some extent, and the dispersion tends to be somewhat higher in populations with a low mean consumption (Bruun et al., 1975). Consequently, the distribution of consumption and the prevalence of excessive drinking in a population is not precisely predicted by the Ledermann model. It should also be noted that the distribution of alcohol may, under certain conditions, deviate significantly from the Ledermann model. According to Thor Norström (1987), this was the case in Sweden during the period of individual rationing of spirits from around 1920 to 1955 when Swedish men were allowed, depending on marital and social status and social stability, a maximum purchase of 1, 2, 3, or 4 liters of spirits per month. Under the rationing, consumption distribution displayed distinct peaks corresponding to the categories of maximum individual rations, and the relative dispersion of consumption was much lower compared to the period after the rationing was abolished. A significant redistribution of alcohol consumption among Swedes occurred after the rationing system ended; the skewness of the distribution increased markedly, revealing a large increase in the prevalence of excessive drinkers.

Ledermann's work has been followed by a large number of empirical studies demonstrating two essential aspects of the distribution of alcohol consumption: (1) that alcohol consumption in various populations and in various eras is indeed very skewed, and (2) that the prevalence of heavy drinkers is linked to the average level of consumption (Bruun et al., 1975; Skog, 1985; Lemmens, 1991;). The strong link between prevalence of excessive drinking and mean consumption in the population implies that the mean consumption is an *indicator* of the prevalence of excessive drinking. Thus, when per capita consumption is high, the prevalence of excessive drinkers is high as well and vice versa. Kettil Bruun and colleagues proposed in 1975 that the proportion of heavy alcohol consumers is approximately proportional to the square of the mean consumption. Consequently, if mean consumption in one population is twice as high as another, a fourfold higher prevalence of heavy alcohol consumers can be expected.

Ledermann did not offer much to explain *why* consumers are distributed along the alcohol consumption scale with such a degree of regularity. (Skog, 1985; Lemmens, 1991). The Norwegian scientist Ole-Jørgen Skog proposed in 1985 a theory of alcohol-consumption distribution: a theory of the collectivity of drinking cultures, founded on two basic hypotheses about human drinking behavior. First, the factors influencing a person's drinking behavior tend to combine multiplicatively, implying that a change in consumption is proportional to the initial consumption level. And second, social interaction is one of the most important mechanisms regulating individual drinking behavior. Based on a large number of surveys from various drinking cultures with a large variation in mean consumption, Skog in 1985 demonstrated that both the prevalence of excessive drinkers (e.g., those consuming above 10 centiliters of pure alcohol per day) and the consumption in all other consumer groups were strongly associated with the mean consumption of the population. Even the consumption among alcoholics co-varied with the mean consumption in the population. He concluded that there is a strong collective component in human drinking behavior and, consequently, when mean consumption in a population changes, all consumer groups move in concert along the consumption scale. This has also been illustrated by longitudinal data. In 2002 Pia Mäkelä analyzed panel data from Finland covering the years 1968–1969. At that time mean alcohol consumption in Finland increased by 46 percent in one year due to a significant increase in availability of alcohol. Mäkelä found that all consumer groups increased their consumption and those with higher initial consumption, more so. Whether similar changes also occur in all consumer groups when the total (or mean) consumption decreases is, however, less well studied.

IMPLICATIONS FOR PREVENTION

Ledermann's work has been an important point of departure in the effort to understand the relationship between the total consumption of alcohol in a society and the prevalence of excessive alcohol use. From a prevention point of view, it is relevant that a reduction in the mean consumption will reduce the number of excessive or "at risk" drinkers and reduce the overall amount of alcohol-related harm. The prevention of alcohol-related harms, however, is not only about reducing consumption among the heaviest drinkers and those with the highest risks. For several types of alcohol-related harms—particularly acute harms, such as accidents and violence—the majority of cases are not found among the relatively few excessive drinkers, but mainly among low- or moderate-risk drinkers according to Skog's 2006 study. In such cases the potential impact of population-based prevention strategies is larger than that of strategies aimed at a small group of high-risk individuals. In 1981 Geoffrey Rose referred to this as the *prevention paradox.*

Based on what is known about the total consumption model and the prevention paradox, good arguments can be made for applying prevention strategies to reduce total consumption (or mean consumption) of alcohol in a population. Not only will reduced total consumption imply less harm as excessive drinkers become fewer, but it will also imply less harm among the light and moderate drinkers, because these groups will also drink less. The empirical evidence to support these assumptions is found in numerous studies demonstrating that some population-based prevention strategies (those that affect all consumers), such as price and availability of alcohol, are effective in reducing not only total consumption but also the amount

of alcohol-related harm, according to work by Thomas Babor et al. in 2003. Mäkelä, Ingeborg Rossow, and Kalle Tryggvesson present further evidence for the effectiveness of such strategies among heavy drinkers in their 2002 review of differential effects of alcohol policies in the Nordic countries. Many studies indicate that, when availability of alcohol changes, those with an initially high level of consumption are most affected.

As Babor and his colleagues pointed out in 2003, several decades of research have clearly shown that the amount of alcohol-related harm in a population is not only proportional to the total consumption of alcohol but also to the way in which alcohol is consumed. Thus, in 2002 Norström and others indicated that the same amount of alcohol may cause more harm in a population with a drinking pattern characterized by relatively few, but heavy, drinking occasions as compared to a population where the intake is less per occasion and spread over a larger number of drinking occasions. Thus effective strategies to prevent heavy drinking occasions and to prevent drinking in risky contexts are important supplements to those aimed at reducing total consumption.

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PRISM. The Psychiatric Research Interview for Substance and Mental Disorders (PRISM) (Hasin et al., 1996; 2006) is a semi-structured diagnostic interview designed expressly to assess DSM-IV psychiatric disorders in individuals who abuse alcohol and drugs. The PRISM is most useful when a psychiatric diagnosis is needed for research purposes, intake assessment, or treatment planning. One challenge in psychiatric diagnosis has been to design a measure to differentiate three conditions: (a) expected effects of intoxication and withdrawal, (b) psychiatric disorders occurring during periods of heavy substance use, and (c) psychiatric disorders that are clearly independent from substance use. In the PRISM, a substance-induced diagnosis is given if the episode co-occurs with heavy substance use and the individual experiences symptoms that are greater than the expected effects of intoxication or withdrawal. The instrument's strength is in differentiating primary psychiatric disorders, such as major depression, from psychiatric syndromes that overlap with periods of heavy substance use or withdrawal.

The PRISM provides current and lifetime diagnoses that commonly occur with heavy substance use: mood and anxiety disorders. Modules are also

provided to assess psychotic disorders, eating disorders, and antisocial and borderline personality disorders. Special assessment procedures are included for disorders that can mimic intoxication and withdrawal states (depression, mania, dysthymia, psychosis, panic, generalized anxiety) to rule out physiological symptoms associated with heavy substance use.

The substance modules consist of a brief screening for use of alcohol and seven drug categories (cocaine, heroin, cannabis, hallucinogens, sedatives, stimulants, and opiates), chronic intoxication and binge use, and the time period in which substance use occurred (last 12 months, prior to last 12 months). If the respondent passes screening for alcohol or drugs (drank or used at least six times in a year), abuse and dependence are assessed independently. Ages of lifetime onset, remission, recurrence, and offset of the most recent episode are obtained for substance-specific abuse and dependence diagnoses.

A number of features were incorporated into the PRISM to reduce the lengthy administration time associated with standardized diagnostic interviews:

- Diagnostic sections are modular so that the instrument can be tailored to fit specific treatment or research needs.
- The Overview section covers basic demographics and a brief history of treatment. Demographic information is limited to marital, educational, housing, military, legal, and employment status. Medical and psychiatric treatment items inquire about lifetime major medical conditions, and earliest and most recent psychiatric and substance abuse treatment.
- The substance screening module is placed at the beginning of the interview to provide a background for the assessment of co-occurring psychiatric disorders, thereby limiting substance-related questions in later sections.
- Consumption questions in the substance screening module do not seek detailed information about lifetime patterns of use. Questions are limited to determine if the respondent used a substance at least six times in a single year and whether he or she ever experienced chronic intoxication or binge use.
- Assessment of Major Depressive Disorder begins with the most recent episode. If this episode meets DSM-IV criteria for major depression, a potential earlier substance-induced episode is also explored. Conversely, if the most recent episode is determined to be substance-induced, a potential earlier primary episode is also explored. This way, time is not spent assessing the same type of depressive episode (primary or substance-induced) more than once.

The complete PRISM takes approximately two hours to administer but the time required varies with the complexity of the diagnosis, the number of drugs used, the experience of the interviewer, and the respondent's reporting style. Individuals with clinical experience are better equipped to administer the interview but lay interviewers with proper training and supervision can obtain reliable diagnoses in a timely manner.

RELIABILITY

The PRISM has been subjected to reliability and validity testing. A reliability study (N=285) in which heavy substance users were interviewed twice (each time by a different interviewer) showed good-to-excellent reliability for most substance dependence diagnoses (Hasin et al., 2006). Reliability was also good to excellent for current and lifetime primary (independent) major depression and substance-induced major depression. The reliability of current and lifetime primary anxiety disorder (any anxiety disorder) was fair to good; however, the reliability of substance-induced panic and substance-induced generalized anxiety disorder (GAD) was poor. The reliability of substance-induced generalized anxiety disorder appeared to have been reduced by inconsistencies in reporting of major depressive disorder in the first and second interviews, which led to inconsistent skipping out of the GAD module. Reliability of any current primary or substance-induced psychotic disorder was excellent. An independently conducted validity study compared diagnoses formulated using a Spanish version of the PRISM (Torrens et al., 2004), the Structured Clinical Interview for DSM-IV Diagnosis (SCID-IV), and expert diagnosis made by an experienced clinician using all available data (LEAD [longitudinal expert, all data]; Spitzer, 1983). In that study, concordance between the PRISM and LEAD diagnoses for current depression, past substance-induced major depression, and borderline personality disorder was better than the

concordance between the LEAD procedure and the SCID. Concordance of the three methods for substance dependence was good to excellent. As with all self-report measures, the credibility of the information obtained using the PRISM is susceptible to the respondent's mood at the time of the interview and other cognitive biases.

The PRISM has been used in cross-sectional and longitudinal studies that require the differential diagnosis of primary and substance-induced disorders. Populations of these studies include first-break psychotic patients interviewed in emergency departments (Caton et al., 2005; 2006; 2007), substance abuse patients in inpatient and outpatient treatment settings (Hasin et al., 2002; Aharonovich et al., 2002, 2005; Nunes et al., 2006), Spanish drug abusers in a detoxification unit of a general hospital (Nocon et al., 2007), an HIV-infected cohort (Morgello et al., 2006), Spanish heroin users aged 18 to 30 outside the healthcare system (Rodriguez-Llera et al., 2006), jail recidivists (Chandler & Spicer, 2006), and patients with co-occurring alcohol dependence and depression (Kranzler et al., 2006).

The English paper version of the PRISM and training information can be downloaded at http://www.columbia.edu/~dsh2/prism. A computer-assisted version administered by the interviewer will include marijuana withdrawal (in preparation of DSM-V), and modules for nicotine-related disorders, pathological gambling, and attention deficit hyperactivity disorder (ADHD) (available in 2008). Translated paper versions are available in Spanish (Spain) and Norwegian.

See also **Addictive Personality and Psychological Tests; Alcohol Use Disorder Identification Test (AUDIT); Alcohol, Smoking and Substance Involvement Screening Test (ASSIST); Drug Abuse Screening Test (DAST); Michigan Alcoholism Screening Test (MAST).**

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SHARON SAMET

PRISONS AND JAILS. Jails are typically operated by municipalities or counties and used to confine people on a pre-trial basis or for short sentences, usually for minor offenses. Prisons are operated by state and federal governments and house inmates who have been sentenced for more than a year and who have generally committed offenses that are more serious. Jails and prisons have grown significantly in the past 20 years because of increased drug-related arrests, mandatory sentencing guidelines, and the erosion of community services. The jail population in the United States increased from 405,000 in 1990 to 723,000 in 2008, and the prison population increased from 793,000 to 1,596,000 during this same period (Warren, 2008). The United States has historically imprisoned a large proportion of its population and now has the highest incarceration rate in the world (Sheldon, 2004; Walmsley, 2007). Approximately 2.3 million people were incarcerated in federal or state prisons and local jails in 2008, amounting to an incarceration rate of 1 in every 100 adults (Warren, 2008). Over 3 percent of the U.S. adult population is under some form of correctional supervision, including probation and parole.

Drug offenders account for approximately half of the recent growth in U.S. jails and prisons (Harrison & Beck, 2006) and have high rates of recidivism and reincarceration. Substance use disorders do not resolve simply through forced abstinence in jails and prisons, and incarceration appears to have little effect in reducing drug use and drug-related crime. In fact, states with higher rates of incarceration also tend to have higher rates of drug use (Schiraldi, Holman, & Beatty, 2000). Within the first year after release, 85 percent of offenders with substance use disorders return to drug use, and 95 percent return to drug use within three years (Inciardi, Martin, & Butzin, 2004).

A disproportionate number of people incarcerated on drug offenses are African American and an increasing number are women (Beatty, Petteruti, & Ziedenberg, 2007; Harrison & Beck, 2006). Many drug offenders do not have extensive criminal records and are incarcerated for minor offenses (e.g., drug possession, sales of small quantities of drugs) that do not involve violence or sophisticated criminal activity. Drug offenders are often imprisoned because of the enforcement of minimum mandatory sentences, and many could be placed in less restrictive settings; however, there is an absence of community diversion programs that involve supervision and treatment (Peters & Wexler, 2005).

EXPENSE OF INCARCERATION

The costs associated with expanding jail and prison capacity in the United States are substantial. Total spending on state corrections rose from $12 to $49 billion from 1987 to 2007, and these costs are expected to rise by another $25 billion by 2011 (Warren, 2008). The average cost for incarcerating someone is from $20,000 to $23,000 (Office of National Drug Control Policy, 2001). The costs for incarceration are over six times higher than the costs for providing probation or parole supervision in the community (Administrative Office of the U.S. Courts, 2005). Almost 80 percent of correctional costs are linked to substance abuse, representing approximately 10 times the amount that states currently spend on substance abuse treatment, prevention, and research (National Center on Addiction and Substance Abuse, 2001; Office of National Drug Control Policy, 2001).

RATE OF DISORDERS

At least half of all inmates have a lifetime history of substance use disorders, including a significant

proportion that has a diagnosable substance dependence disorder (Mumola & Karberg, 2006; Peters et al., 1998). These rates are significantly higher than in the general population. Rates of mental disorders, HIV/AIDS, hepatitis, and tuberculosis are also significantly higher among offenders. Many offenders have not previously received adequate treatment for substance abuse, mental health, dental, or other health-care problems, and a significant number have acute and severe health-care needs. Incarceration in jail or prison provides a critically important opportunity to address these health-care issues through treatment services that promote significant lifestyle change and that encourage abstinence, gainful employment, and successful reentry to society.

TREATMENT SERVICES IN JAILS AND PRISONS

In recent years there has been an emerging gap between the need for substance abuse treatment in jails and prisons and the services provided in these settings. Although correctional treatment services have increased during this period, they have not kept pace with the rapid influx of drug offenders, the vast majority of whom are in need of these services. Only a fraction of incarcerated offenders who need these services receives drug treatment. Recent surveys indicate that only 33 percent of jails and 56 percent of prisons provide any type of substance abuse treatment services (Substance Abuse and Mental Health Services Administration, 2000, 2002). When correctional treatment is provided it is often not comprehensive in scope and, it is frequently not provided in treatment units that are isolated from the general inmate population. One of the most significant gaps in services occurs following release from jail or prison, or reentry to the community—a particularly vulnerable time when offenders are exposed to various risks for relapse, and stress associated with reengagement with family, and full-time work (Peters & Bekman, 2007; Peters & Wexler, 2005). Few jails and prisons currently provide reentry services for offenders who are in need of substance abuse services (Cropsey, et al., 2007; Peters, Matthews, & Dvoskin, 2005).

Incarceration in jail or prison provides an opportune time to intervene with drug-involved offenders. Arrest and incarceration often precipitate a crisis in the offender's life and can provide additional motivation to initiate lifestyle changes that have been neglected in the past. The lengthy period of incarceration also provides sufficient time to engage inmates in assessment, treatment, and reentry planning. An important challenge in providing treatment in jails and prisons is that security issues often receive priority over rehabilitation and treatment needs in these settings (Peters, Matthews, & Dvoskin, 2005). Jails and prisons are also not architecturally designed to provide treatment and may have limited space in which to provide these services.

Research indicates that jail and prison treatment can significantly reduce substance abuse, criminal recidivism, and recommitment to prison, particularly when in-custody treatment is coupled with post-release treatment in the community (Inciardi, Martin, & Butzin, 2004; Prendergast et al., 2004). A growing body of research demonstrates that effective drug treatment services for offenders combines behavioral and pharmacological approaches, and encourages sustained involvement over time to address the chronic, relapsing nature of substance use disorders (National Institute on Drug Abuse, 2000).

See also **Crime and Drugs; Criminal Justice System, Treatment in the; Prisons and Jails, Drug Treatment in; Shock Incarceration and Boot-Camp Prisons; Treatment Accountability for Safer Communities (TASC).**

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PRISONS AND JAILS, DRUG TREATMENT IN. Prison and jail populations in the United States have swelled to over two million as a result of a significant increase in arrest and incarceration of drug offenders (Warren, 2008). The vast majority of inmates have significant substance abuse problems, and over one-fourth are arrested for drug offenses (James, 2004; Harrison & Beck, 2004; Peters & Wexler, 2005). Lifetime prevalence rates for substance use disorders among prisoners are between 68 and 74 percent, including 46 percent for drug dependence and 37 percent for alcohol dependence (Karberg & James, 2005; National Institute of Justice, 2000). Additionally, as many as 15 percent of inmates have major mental disorders, rates that are significantly higher than in the general population (Ditton, 1999; National GAINS Center, 2004). Approximately two-thirds of drug-involved offenders are rearrested within three years of release from custody (Langan & Levin, 2002).

As of 2008, a growing gap existed between the need for drug treatment in correctional settings and the scope of the services provided. Among inmates with substance use disorders only 17 percent received treatment in prisons or jails, with only 7 percent receiving treatment in jails (Karberg & James, 2005). Fewer than 40 percent of all correctional facilities provide substance abuse treatment (Substance Abuse and Mental Health Services Administration, 2000), and less than 6 percent of state and federal prison budgets as of 2008 was spent on substance abuse treatment. Of significant concern is the absence of reentry or transition services for substance-involved inmates who are returning to the community (Travis, Solomon, & Waul, 2001), a period marked by elevated risk for relapse and recidivism.

Many prison and jail substance-abuse programs are provided in settings that are not conducive to effective treatment, are not comprehensive in approach, and are poorly staffed (Peters, Matthews, & Dvoskin, 2005). For example, many such programs rely on volunteers, non-licensed staff, or inmate counselors. Similarly, staff/inmate ratios are quite low in many correctional drug treatment programs, averaging 1:25 in state prisons (Substance Abuse and Mental Health Services Administration, 2002). A survey conducted through CJ-DATS network of the National Institute on Drug Abuse (NIDA) indicates that while specialized prison-based treatment programs are available, a significant proportion of assessment and treatment services for substance-involved inmates are "generic" and inadequate in scope and quality (Cropsey et al., 2007).

Correctional drug treatment programs were first developed in the United States in the late 1920s for opiate addiction. During the 1960s several states enacted civil commitment statutes that provided substance abuse treatment in secure residential settings. A common modality of correctional residential treatment that emerged at this time was the therapeutic community (TC), which is based on a social learning model and engages professional staff and a peer recovery community to promote behavior change. There is considerable evidence to support the effectiveness of prison TCs in treating substance use disorders (Pearson & Lipton, 1999).

Subsequently, some jails and prisons developed multitiered substance abuse treatment services that include outpatient, intensive outpatient, short-term residential, and reentry/transition programs, in addition to TCs (Peters, Matthews, & Dvoskin, 2005). For example, the Federal Bureau of Prisons and a number of state prison systems developed a continuum of treatment services that vary in length and intensity to meet the needs of substance-involved offenders (Peters, Matthews, & Dvoskin, 2005; Weinman & Dignam, 2002). Several specialized correctional programs were also developed for inmates with co-occurring substance use and mental disorders (Peters & Bekman, 2007). Correctional treatment programs introduced in other countries include *harm reduction* approaches and treatment interventions (e.g., cognitive-behavioral and psychosocial skills programs) that are designed for application with a broader inmate population (Jacob & Stover, 2000; Lightfoot, 1999). Most comprehensive substance abuse treatment programs in jails and prisons employ the following types of evidence-based services: (1) screening and assessment, (2) motivational interviewing, (3) cognitive skills training and criminal thinking, (4) relapse prevention, and (5) re-entry and transition planning.

Several challenges arise in providing substance abuse treatment in prisons and jails. Jails house many unsentenced inmates for short periods of time who may be reluctant to accurately disclose information that could adversely influence their pending case and who may be less interested in treatment than in a favorable judicial disposition. Noise levels and lack of adequate space present barriers to effective treatment in many correctional facilities. In addition, the primary focus for most correctional systems is inmate security and punishment rather than rehabilitation of substance use disorders. In times of budget cutbacks, substance abuse services are often among the first to be eliminated. Prisons and jails vary widely in the resources allocated for substance abuse treatment and are often influenced by cyclical patterns of political support for either punishment or rehabilitation of offenders.

Considerable evidence indicates that correctional treatment reduces drug use and criminal activity. Research indicates that these programs lead to significant reductions in arrests, recommitment to prison, and substance abuse during 12- and 24-month follow-up periods, although positive gains related to prison treatment are not typically maintained during three- and five-year follow-up periods (Martin et al., 1999; Prendergast et al., 2004; Wexler et al., 1999a, 1999b). However, long-term positive outcomes have been found among offenders who participate in prison treatment that is followed by aftercare treatment in the community (Inciardi, Martin, & Butzin, 2004; Martin et al., 1999; Prendergast et al., 2004). Research also indicates that providing a continuum of offender substance abuse treatment services during custody and in the community effectively reduces costs associated with crime and incarceration (McCollister et al., 2003).

While the courts have consistently rejected a general constitutional right to drug treatment in prisons and jails, case law indicates that some services are

legally mandated. For example, inmates have the right to medical treatment to address withdrawal (i.e., detoxification) and other serious, life-threatening medical problems associated with substance abuse. A number of professional standards have also been developed to guide the implementation of correctional substance abuse treatment services, including those developed by the National Commission on Correctional Health Care (NCCHC, 2008) and by the American Correctional Association (ACA). Essential substance abuse treatment services described in professional standards for both jails and prisons include management of intoxication and withdrawal and a comprehensive health assessment that includes a substance abuse history.

See also **Coerced Treatment for Substance Offenders; Treatment, Stages/Phases of: Aftercare.**

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PRISONS AND JAILS, DRUG USE AND HIV/AIDS IN. Human immunodeficiency virus and acquired immunodeficiency syndrome, commonly abbreviated as HIV/AIDS, have had a serious impact on U.S. prisons and jails since the 1980s and represent a dangerous health threat among all inmate populations and for the general public when offenders are released from custody. Of the approximately 2.3 million persons in U.S. prisons and jails, between 1 to 2 percent are estimated to be infected with HIV (Hammett, Harmon, & Maruschak, 1999; Maruschak, 2008). These rates are significantly higher than in the U.S. general population (Bick, 2007; Maruschak, 2008).

INFECTED INCARCERATED PERSONS AND THEIR TREATMENT

An estimated 25 percent of HIV-infected persons in the United States are incarcerated in prison or jail during a given year (Hammett, Harmon, & Rhodes, 2002; Spaulding et al., 2002). HIV/AIDS prevalence rates in prisons and jails vary widely by geographic area and gender, with the highest rates (3.6%) reported in the Northeast and the lowest rates in the Midwest and West. HIV/AIDS is more frequently detected among female inmates (2.4%) than male inmates (1.6%), and disproportionately affects minorities (Foundation for AIDS Research, 2008; Maruschak, 2008). The number of HIV/AIDs cases and the mortality rate in prisons decreased in the late 1990s and early 2000s, reflecting similar trends in the general population (Bick, 2007; Maruschak, 2008).

Advances in medication therapy have significantly reduced AIDS-related mortality rates in prisons and jails, reflecting declines in the general population (Baham et al., 2002). Inmates have a constitutional right to HIV treatment and other medical care for life-threatening illnesses. However, in some settings, inmates are treated for HIV and related disorders by staff who do not have specialized training related to HIV/AIDS, drug treatment, mental health services, or reentry services (Foundation for AIDS Research, 2008). Privatization of correctional healthcare services and rising costs for correctional medical treatment have also presented barriers to implementation of effective services (DeGroot, Hammett, & Scheib, 1996).

DRUG ABUSE, HIV/AIDS, AND PREVENTION STRATEGIES

There is a strong connection between drug abuse and HIV/AIDS in correctional settings, affecting strategies for both prevention and treatment. Inmates have higher rates than the general population of sexually transmitted diseases, other infectious disease (e.g. hepatitis, tuberculosis), substance use, and mental disorders that facilitate the spread of HIV (Foundation for AIDS Research, 2008). For example, as many as three-fourths of offenders have diagnosable substance use disorders (Karberg & James, 2005), including many who have a history of IV drug use and risky sexual behavior that is related to drug use. Drugs are widely available in prisons and jails, and HIV is often spread through injection drug use in these settings. Two other major routes of HIV transmission in correctional settings are sexual behavior and tattooing (Zack, 2007).

The often lengthy period of incarceration offers significant opportunities to prevent HIV through medications, substance abuse treatment, and other means (Beckwith et al., 2006). Inmates often come from impoverished, medically underserved neighborhoods, and have not frequently engaged in drug treatment, received HIV screening or other prevention services, or received HIV treatment (Foundation for AIDS Research, 2008, Peters & Wexler, 2005; Zack, 2007). Although drug treatment is available in many prisons and jails, these services are provided to only a small proportion of those inmates who have substance use disorders (Karberg & James, 2005). When correctional drug treatment is available, services are not typically prioritized for inmates with HIV/AIDs, and HIV prevention practices are often not comprehensively addressed.

Substance abuse treatment has been shown to be effective in reducing drug and alcohol use and risky sexual behavior among offenders and to prevent HIV infection (Prendergast, Urada, & Podus, 2001; Sorensen & Copeland, 2000; World Health Organization, 2004) and is clearly an underused prevention strategy. Substance abuse treatment has significant positive effects on knowledge, attitudes, and beliefs related to HIV prevention; sexual behavior; and particularly on risk reduction skills (Prendergast et al., 2001). Research indicates that methadone maintenance also has a significant impact on HIV risk behaviors and helps to prevent HIV infection (Sorensen & Copeland, 2000). Drug testing in correctional settings provides additional deterrence for intravenous (IV) and other drug use and can help to identify offenders who are in need of treatment and supervision.

Other important HIV prevention and treatment strategies implemented in prisons and jails include routine HIV screening, which has proven to be cost-effective in prisons and other settings (Bick, 2007; Sanders et al., 2005; Varghese & Peterman, 2001). Identification of HIV status through screening can facilitate referral to counseling, promotion of testing for others who may be at risk, and can reduce HIV risk behaviors (Centers for Disease Control and Prevention, 2000). Mandatory HIV testing is provided by almost half of the state prison systems (Bick, 2007). However, this approach has been criticized due to the potential for discrimination and segregation of HIV-infected inmates (World Health Organization, 2006), leading to reduced access to housing options and educational and job opportunities. In jails, the lengthy period of time required to test blood samples for HIV and to return results can be problematic for a significant number of inmates who are released within two weeks of arrest.

INTERVENTIONS FOR POST-CUSTODY POPULATIONS

Several HIV interventions have proven effective in reducing post-custody HIV risk behaviors (Wolitski, 2006; Zack, 2007), including educational services, development of risk reduction plans, and reentry services (e.g., case management, housing, employment). Basic information about HIV is an important first step in educating inmates about prevention approaches and is often provided in jail booking or general confinement settings and at the time of prison reception. However, educational approaches are insufficient to generate changes in HIV risk behaviors, and lasting behavior change requires use of professional staff and interventions focused on rehearsal, modeling, and feedback related to specific HIV prevention skills (Zack, 2007). A number of *harm reduction* approaches (e.g., condom distribution, syringe exchange) have been successfully used in European prisons to prevent HIV transmission (Dolan, Rutter, & Wodak, 2003), although these are only used in a few U.S. prisons and jails. In general, opportunities to participate in HIV education, prevention, and treatment interventions should be provided throughout the course of incarceration.

The vast majority of prison and jail inmates eventually return to the community. However, release from custody is often associated with worsening of HIV/AIDS symptoms and reengagement in risky behaviors (Stephenson & Leone, 2005). Most jails and prisons do not provide adequate reentry services, leading to resumption of HIV risk behaviors, transmission of HIV, and re-arrest (Health Resources and Services Administration; HRSA, 2007; McLean et al., 2006). Difficulties in reinstating medical benefits and lack of access to health insurance present additional barriers to effective community reentry. Correctional discharge planning and reentry services are of critical importance to ensure continuity of HIV treatment, engagement in substance abuse and mental health

services, and access to housing and educational/vocational services (United Nations Office on Drugs and Crime/World Health Organization, 2006; Zack, 2007). Demonstration projects developed by several state prison systems have provided a combination of pre-release planning, life skills training, substance abuse treatment, peer support, housing and employment support, assertive case management, and linkage to community treatment (HRSA, 2007). Correctional transition planning and case management programs have been shown to significantly reduce risky sexual behavior and criminal recidivism and to facilitate involvement in substance abuse treatment and healthcare services among offenders with HIV (Bick, 2007; Myers et al., 2005; Rich et al., 2001, Wolitski, 2006).

See also **See also Alcohol and AIDS; Injecting Drug Users and HIV; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Substance Abuse and AIDS.**

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PROCESSES OF CHANGE MODEL.

Traditionally, changing an addictive behavior was assumed to be the same as taking action. People with addictions were viewed as changing when they quit abusing substances. Action-oriented therapies have been readily available and have dominated the ways in which individuals and addiction practitioners perceive behavioral change. In other words, motivation to change was seen as a *fixed* state; individuals who were motivated to change could make changes, and intervention was unlikely to be effective among those who were not motivated.

FIVE STAGES FOR BEHAVIORAL CHANGE

Based on smoking cessation research conducted in the 1970s, James Prochaska and Carlos DiClemente (1983; 1984; 1998) proposed a model of behavioral change: the Transtheoretical Model (TTM). According to this model, behavioral change is a process, which unfolds over time and involves progress through five stages of change: Precontemplation, Contemplation, Preparation, Action, and Maintenance. "The underlying perspective of the stages of change is that there is a multidimensional process of intentional behavior change that extends from the establishment of a stable pattern of abuse to the achievement of significant sustained change of the addictive behavior" (DiClemente et al., 2004, p. 104). The word *intentional* underlines the important role that motivation plays at each stage of change. Since the inception of TTM, it has received substantial empirical support that applies to a wide range of behavior, populations, and settings.

Precontemplation State and Stage Matching. In the Precontemplation stage, individuals do not intend to take action in the foreseeable future. They may or may not be aware of their problem behavior and have little or no interest in change. Families, friends, or employers, however, are often well aware that precontemplators have problems. When precontemplators present for addiction treatment, they often do so because of pressure from others. These individuals are at risk of dropping out of treatment quickly and prematurely. The research of Prochaska and colleagues has shown that if therapists match interventions to the individual's stage, precontemplators will complete treatment at the same rate as those in the Preparation stage.

Stage matching begins by setting realistic goals. If precontemplators are pressured into immediate action, they are more likely to drop out of treatment. In contrast to traditional action-oriented treatment in which therapists tend to label such individuals as unmotivated or noncompliant, the TTM provides a different approach in conceptualizing behavioral change to meet the needs of these individuals.

The goal of addiction treatment with precontemplators is to help them progress to Contemplation. This initial goal produces success early in treatment. Consciousness-raising (see Table 1) is frequently used to help individuals become more aware of why

Process	Definitions: Interventions
Consciousness raising	Increasing information about self and problem: observations, confrontations, interpretations, bibliotherapy
Self-reevaluation	Assessing how one feels and thinks about oneself with respect to a problem: value clarification, imagery, corrective emotional experience
Self-liberation	Choosing and commitment to act or belief in ability to change: decision-making therapy, New Year's resolutions, logotherapy techniques, commitment–enhancing techniques
Counterconditioning	Substituting alternatives for problem behaviors: relaxation, desensitization, assertion, positive self-statements
Stimulus control	Avoiding or countering stimuli that elicit problem behaviors: restructuring one's environment (e.g., removing alcohol or fattening foods), avoiding high–risk cues, fading techniques
Reinforcement management	Rewarding one's self or being rewarded by others for making changes: contingency contracts, overt and covert reinforcement, self-reward
Helping relationships	Being open and trusting about problems with someone who cares: therapeutic alliance, social support, self-help groups
Dramatic relief	Experiencing and expressing feelings about one's problems and solutions: psychodrama, grieving losses, role playing
Environmental reevaluation	Assessing how one's problem affects physical environment: empathy training, documentaries
Social liberation	Increasing alternatives for nonproblem behaviors available in society: advocating for rights of repressed, empowering, policy interventions

Table 1. Titles, definitions, and representative interventions of the processes of change. (Source: Prochaska, DiClemente, & Norcross, 1992.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

they are not ready to change problem behavior. As precontemplators become more aware of why they are resistant to change, they are more likely to consider the pros of treatment. As the pros of change increase, individuals are more likely to progress into Contemplation.

Contemplation. In the Contemplation stage, awareness of the pros of change increase, but the cons also increase. The pros and cons of behavioral change, conceptualized as decisional balance in the TTM, produce a profound ambivalence that causes some individuals to procrastinate. This ambivalent attitude toward using substances can sometimes mislead addiction practitioners into assuming that these individuals are ready for immediate action. For individuals to progress to Preparation, their perception of the cons of quitting must change. They need to reevaluate how they think and feel about themselves as an addict and how they imagine themselves free from addiction.

Individuals' cons of change have to decrease only about half as much as their pros increase; therefore, in stage-matched treatments researchers place twice as much emphasis on the benefits of changing. Typically, there are more than forty scientific benefits to becoming free from an addiction. One of a few strategies to enhance motivation is to become aware of how much of one's body, self, social relations, and society benefit from such major changes.

Preparation. Individuals in the Preparation stage are convinced the pros of changing outweigh the cons. They are generally ready to take immediate action within thirty days and often have a plan for action. However, they might not be fully committed to their plan due to a number of reasons such as low self-efficacy (lack of confidence in the ability to change across problem situations). For these individuals, action-oriented treatment programs may effectively help them progress to the next stage.

Action. In the Action stage, individuals take specific steps to implement their plans for changing their substance use behavior. Individuals need to be prepared for how long action will last. Biologically, going through the symptoms of withdrawal is relatively quick. Behaviorally, however, people have to be prepared to work on changing their behavior for about six months.

Maintenance. Individuals progress into the Maintenance stage when the new behavior becomes the norm. In this stage, individuals establish a new pattern of behaviors for at least six months, and this change eventually can lead to termination of the change process. Evidence suggests that the Maintenance stage lasts four to five years. With smoking, for example, the national data in the 1990 *Surgeon General's Report* indicated that after 12 months of not a single puff, the percentage of smokers who resume regular smoking is about 40 percent. After

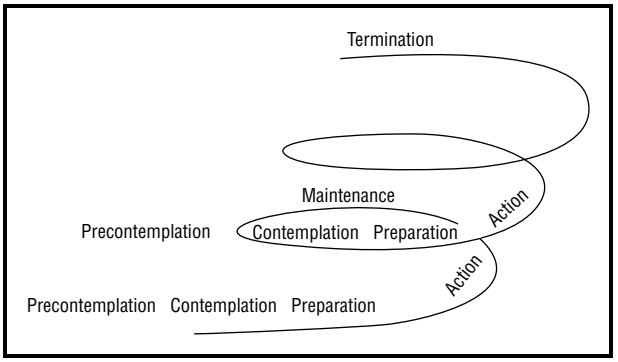

Figure 1. A spiral model of the stages of change. (Source: Prochaska, DiClemente, & Norcross, 1992.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

five years of total abstinence, the relapse rate drops to 5 percent.

DIFFERENT PATHS FOR CHANGE

A spiral model of the Stage of Change is presented in Figure 1 to illustrate how most individuals travel through the stages of change. Behavioral change in this model is viewed as a process: "Current stage status represents a changeable state rather than a static trait" (DiClemente et al., 2004, p. 108). The duration in which each individual occupies each stage can vary. For example, after learning about the death of a friend from liver failure, an individual who is in Precontemplation about reducing alcohol consumption today could be in the Preparation or Action stage tomorrow.

Furthermore, individuals can move through stages in both linear and nonlinear fashions, with nonlinear being more common. When individuals go back to an earlier stage of change, regression occurs. In general, people can regress from any stage to an earlier stage. One form of regression is relapse, which involves regression from Action or Maintenance to an earlier stage. In a study examining smoking behavior (Prochaska & DiClemente, 1986), only about 15 percent of participants regressed all the way to the Precontemplation stage. The vast majority of participants regressed to the stage of Contemplation or Preparation. According to the TTM, relapse is perceived as a positive opportunity, rather than a failure to change problem behavior: "Movement back and forth, as well as recycling through the stages, represents a successive learning process whereby the individual continues to redo the tasks of various stages in order to achieve a level of completion that would support movement toward sustained change of the addictive behavior" (DiClemente et al., 2004, p. 104).

In addition to Stages of Change, Prochaska and colleagues (1992) proposed that ten covert and overt processes need to be implemented to successfully progress through the stages of change and attain the desired behavioral change (see Table 1). These processes of change aim to explain how changes in cognition, emotion, and behavior take place. These ten processes can be divided into two groups: cognitive and affective experiential processes and behavioral processes. Experiential processes refer to consciousness raising, dramatic relief, environmental reevaluation, social-liberation, and self-reevaluation. Behavioral processes include counterconditioning, stimulus control, reinforcement management, helping relationship, and environmental evaluation. To understand how and when behavioral change occurs, Prochaska and colleagues (1992) integrated both processes and stage of change in their research. For example, for smoking cessation and weight loss, they found that individuals who were in Precontemplation used eight of the change processes significantly less than those who were in any other stages.

ASSESSMENT OF CORE CONSTRUCTS

Between the late 1970s and the early 2000s, Prochaska and DiClemente developed measures to assess core constructs of the TTM: the stages of change, decisional balance, processes of change, temptations, and self-efficacy. Critics raised questions regarding the validity of this model, particularly in how to assess stage status of individuals with different substance abuse problems and in different types of treatment programs. In an effort to address these concerns, DiClemente and colleagues (2004) identified key issues in assessing stage status. For example, one key issue is the difficulty in capturing stage status, given that it signifies a changeable state and not a static trait. In addition, they highlighted the importance of understanding motivation in terms of the stages of change:

> The stages of change specify motivational demands by segmenting the change process into specific tasks to be accomplished and goals to be achieved, if movement toward successfully sustained change is to occur. Each of the multiple tasks encountered on the road to recovery requires effort, energy, and

> 'motivation' on the part of the addicted individual. Successful change of an addiction represents a resolution of each stage's tasks in a way that supports engagement in the tasks of the next stage. (DiClemente et al., 2004, p. 104)

DiClemente and colleagues recommended that more research is needed to develop better assessments as well as enhance the understanding of subtasks at each stage.

See also **Treatment, Behavioral Approaches to: An Overview.**

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PRODUCTIVITY: EFFECTS OF ALCOHOL ON. Alcohol is the most commonly used and abused substance in the United States. As with workforce drug use, besides affecting productivity, the depressant effects of alcohol impact workplace safety because its use may reduce an individual's reaction time, and impair judgment and memory. Its use also affects workplace morale because of attendance and coworker relationship problems. Its use also adds to the health costs of employers. The impact from alcohol occurs not only as a consequence of intoxication, but also because of carry-over effects in the short term such as a hangover, and chronic health effects such as alcoholism or liver disease.

In 2000 the National Household Survey on Drug Abuse revealed that for the reported workforce of over 108 million people aged 18 to 48, about 8 percent reported they had been drinking heavily (five or more drinks on five or more occasions) during the past month and 7.4 percent of these workers were dependent on or abusing alcohol. Heavy drinking is more than three times as prevalent among male workers than it is among female workers, and it is most prevalent in semiskilled or male-dominated occupations such as construction, mining, precision production and craft, and operators and fabricators. Younger workers (aged 18 to 25) are over two times more likely to be heavy drinkers than older workers (aged 35 to 49) (The George Washington University Medical Center, 2002).

Problem drinkers (individuals who are not necessarily alcoholics but are heavy or binge drinkers prone to causing harm or conflict while under the influence) and alcoholics are more likely than other workers to have major difficulties in the workplace; however, the cost to employers is not limited to problem drinkers and alcoholics, it is also affected by non-drinking employees (The George Washington University Medical Center, 2002). According to the National Institute on Alcohol Abuse and Alcoholism, there are two types of problem drinkers: chronic and situational. Chronic drinkers have been heavy drinkers (2 or more drinks per day on average per year) for many years (FTN Centers For Disease Control And Prevention). Binge drinkers are defined as drinking that corresponds to "5 or more drinks on a single occasion for men or 4 or more drinks on a single occasion for women, generally within about 2 hours" (FTN National Institute of Alcohol Abuse and Alcoholism). Situational abusers may develop a drinking problem later in life, often because of negative life events (failing health, death of a loved one, loneliness) wherein alcohol may initially bring "relief" but may later turn into a problem.

The impact of alcohol use off the job extends to the workplace and affects the user's functionality. Employees who drink heavily off the job are more likely to experience hangovers causing them to be absent, to show up late or leave early; to feel sick at work; to sleep on the job; to perform poorly; or to initiate conflict with their coworkers.

An estimated 500 million workdays are lost annually due to alcoholism (National Association of Treatment Providers, 1991).

Problems related to alcohol and drug abuse cost American businesses over $134 billion annually in lost productivity, and work performance drops significantly (The George Washington University Medical Center, 2002).

Up to 40 percent of industrial fatalities can be linked to alcohol abuse and alcoholism and the individuals who consume alcohol are more likely to cause injuries to themselves or others while on the job (Baker, 1987; Bureau of National Affairs, 1986).

People with alcoholism and problem drinkers are more likely than other workers to have had three or more employers during the last year, to have missed work more than two days in the past month because of illness or injury, and to have skipped work more than two days in the past month, according to the findings of a National Survey on Drug Use and Health taken in 2000. People with alcoholism use twice as much sick leave as other employees (The George Washington University Medical Center, 2002).

Employees who regularly use alcohol are five times more likely to file workers' compensation claims (The George Washington University Medical Center, 2002); nearly half of all workers' compensation claims are related to substance abuse (National Council on Compensation Insurance, 2008).

Employees who use alcohol and other drugs cost their employers about three times as much in medical claims as do employees who do not use drugs or alcohol (Bureau of National Affairs, 1980).

Sixty percent of alcohol-related job performance problems are caused by people who are *not* alcoholics or problem drinkers; they are employees who occasionally drink too much at lunch or the night before. Twenty percent of workers reported that they have been injured, had to cover for a coworker, or had to work harder because of other employees' alcohol consumption (The George Washington University Medical Center, 2002).

As with drugs, many employers implemented workplace alcohol-testing programs using breath alcohol protocols. The Nuclear Regulatory Commission (NRC) and the Department of Transportation (DOT) require alcohol testing as a part of their substance abuse prevention efforts. Because of the rapid elimination of alcohol from the human body, the deterrent nature of alcohol testing is significantly less in these programs than those for drug testing, because evidence of recent drug use remains in the system for a day or more depending on the drug, and frequency and intensity of use. Positive rates for alcohol testing by the NRC and DOT remain low, as is true for most other employers. A more reliable method of alcohol testing is for-cause testing because there is a greater likelihood of recent alcohol use.

See also **Accidents and Injuries from Alcohol; Complications: Medical and Behavioral Toxicity Overview; Economic Costs of Alcohol and Drug Abuse; Industry and Workplace, Drug Use in; Social Costs of Alcohol and Drug Abuse.**

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DICK BUCHER

PRODUCTIVITY: EFFECTS OF DRUG USE ON.

See **Industry and Workplace, Drug Use in.**

PROFESSIONAL CREDENTIALING.

Myriad health-care professionals and paraprofessionals provide treatment for substance-abuse (or SA) disorders. They include, but are not limited to, physicians, psychologists, social workers, nurses and nurse practitioners, clergy, and addiction or drug-abuse counselors. Institutions and programs that train these professionals are accredited, and such individuals, after undergoing training, may obtain credentials from a professional or state body.

Although accreditation applies to programs or institutions and does not cover substance-abuse counseling, credentials apply to individuals and do cover this subspecialty. Institutions that offer training in substance-abuse counseling design their programs to meet the requirements outlined by the state or by potential employers so that graduates can obtain certification. Graduates must then pass tests certifying that they have a specific level of proficiency in the theoretical and practical aspects of substance-abuse treatment. For example, in Michigan the Department of Public Health and other interested organizations initiated a program for the professional development of counselors that is based on education, experience, supervised practical training, professional recommendation, testing and review, ethics, and residence. Michigan requires that persons undergo a three-tier testing process covering the theoretical and practical aspects of substance-abuse treatment to become certified addiction counselors (CACs). The first test covers the fundamental knowledge of substance-abuse counseling; the second, applications to specific populations; and the third, the oral presentation of a case. Certification is for a specific term and renewal requires additional education. Once certified, a person may provide addiction treatment in states other than the one that awarded certification, through a reciprocity agreement that covers states with membership in the International Certification Reciprocity Consortium.

In addition to certification by the state, professional credentialing may also be obtained through professional organizations. For example, the American Society of Addiction Medicine, under the auspices of the American Medical Association, certifies physicians who wish to treat substance abuse. The association offers courses that review topics in addiction theory and practice, examines candidates who wish to obtain credentials, and certifies their advanced knowledge and skills in this area. Other professional associations such as the American Psychological Association are currently developing procedures and mechanisms for providing substance-abuse-treatment credentials to their members who supply mental health services in this area.

Both accreditation and certification work to improve the quality of the education and specialty training that individuals receive and to assure the quality of the services provided. As a safeguard, consumers of substance-abuse services may determine whether the professional delivering the services was trained in a program accredited by the appropriate professional organization in a university or college and accredited by the appropriate regional accrediting board. Consumers may also determine if the professional holds credentials as a substance-abuse counselor, as these credentials certify that a person has met certain educational requirements and displayed the level of knowledge and skill deemed necessary in the profession.

Professional substance-abuse-treatment credentialing is somewhat murky in many states, as professionals who hold a license or certification within their initial discipline (e.g., social work, counseling, or psychology) rarely need to obtain additional substance-abuse certification in order to provide those services. The upshot of this is that many more persons provide substance-abuse services to clients than there are credentialed substance-abuse providers in the United States.

In a 2003 Substance Abuse and Mental Health Services Administration (SAMHSA) Alcohol and Drug Services (ADSS) study, it was reported that between 45 and 72 percent of those providing substance-order services are specifically credentialed to do so, and nearly all are degreed or licensed in related disciplines. In a large-scale study Harwood (2002) found that slightly more than half of the staff at agencies or facilities surveyed were credentialed or licensed specifically as substance-abuse service providers; of those, nearly 60 percent held a master's degree. Among those substance-abuse service providers without credentials or licenses, few had graduate degrees, and nearly two-thirds less than a college education. Roughly one-fourth of the personnel surveyed were neither credentialed nor were they pursuing the process to become so. Among the substance-abuse counselors included in the Harwood study, 15,500 were neither licensed nor certified, and 16,700 of the general behavioral health service providers lacked the credentials to provide substance-abuse counseling services.

The SAMSHA results were similar, indicating that less than half of the staff providing direct substance-abuse counseling and treatment possessed specific credentials for doing so. However, their data indicated significant variation by type of treatment facility, with outpatient, nonmethadone clinics having the highest rate of credentialed or certified staff and methadone-specific clinics the fewest. However, methadone clinics are federally required to have the most staff with medical training, based on their mission. Overall, significantly higher percentages of credentialed substance-abuse counselors were employed by private, not-for-profit or for-profit agencies than by public agencies and facilities. The fewest certified or credentialed substance-abuse counselors were employed by community mental health centers, according to the ADSS/SAMHSA data.

In 2003 the National Association of Alcoholism and Drug Abuse Counselors (NAADAC) reported that 79 percent of its membership were licensed, certified, or credentialed to provide substance-abuse services. It also reported that 31 percent of its membership were licensed professional counselors (LPCs or LPCCs), 22 percent licensed clinical social workers (LCSWs or LISWs), and 16 percent licensed mental health counselors (LMHCs). No statistics were reported on how many of the members hold more than one license or certification, that is, are credentialed in more than one discipline—that percentage is likely to be significant, based on the SAMHSA and Harwood data.

Unlike many of the helping professions, the substance-abuse counseling credentialing process is quite often competency- or experience-based rather than educationally based. For as long as rigorous educational or training standards are not required for service provision, the workforce in the field will lack uniformity of service provision. It would benefit substance-abuse clients significantly to be served by providers who are truly skilled and trained in the field of addiction treatment.

See also **American Society of Addiction Medicine (ASAM).**

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PROHIBITION OF ALCOHOL. The Eighteenth Amendment to the Constitution of the United States, passed by Congress in 1917, had its origins in temperance reformers' efforts to

eliminate the vice and social destruction they believed stemmed from the sale of alcoholic beverages, particularly alcohol sold at saloons. The amendment prohibited the "manufacture, sale and transportation of intoxicating liquors" and became effective one year after its ratification by the states. It outlawed only the manufacture, transport, and sale of liquor; it did not criminalize the possession of alcohol for personal use, nor did it make purchase of liquor from bootleggers a criminal offense, nor did it define "intoxicating" liquors. To implement the amendment, Congress passed the National Prohibition Act, better known as the Volstead Act. The Volstead Act allowed alcohol to be produced and transported for scientific and other commercial purposes. It also defined an intoxicating liquor as any beverage containing more than 0.5 percent alcohol. It could have set the permissible level higher and allowed the production, transportation, and sale of beer, but it did not. Prohibition became effective in 1920.

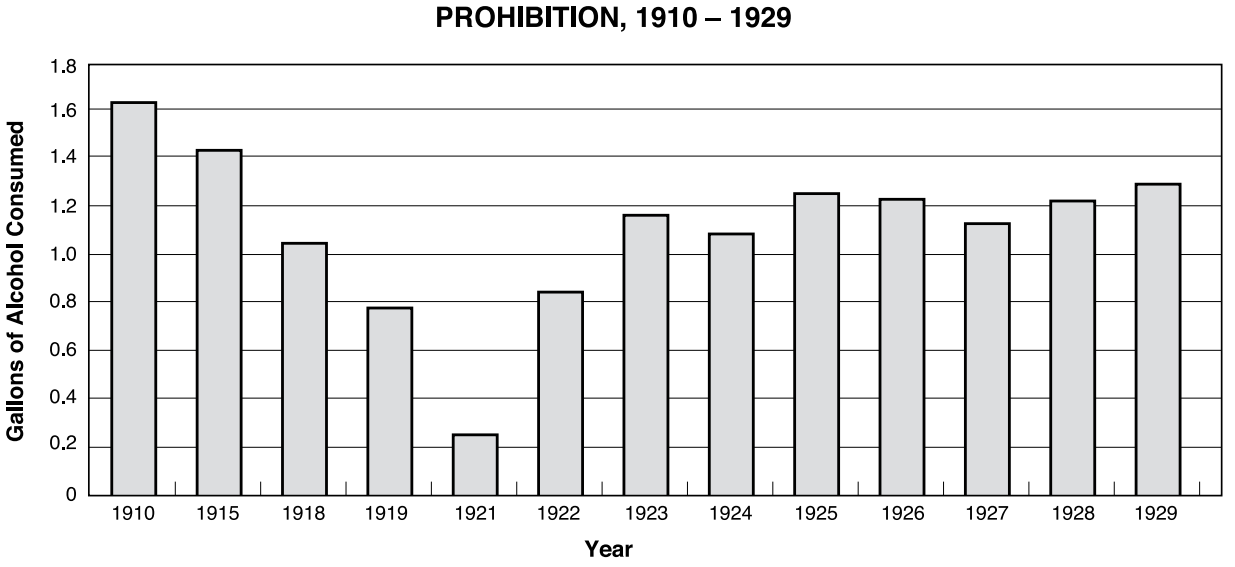
The Treasury Department established a Prohibition Bureau to carry out the provisions of the law. Under the Volstead Act, Treasury agents could obtain a search warrant only if they could prove that alcohol was being sold, thus precluding searches of individual homes, no matter how much liquor might be there. Some wealthy people, given ample notice that Prohibition was coming, laid in enough alcoholic beverages to last them through most of the following decade. The law also had the effect of allowing manufacture for personal use. Such home production sometimes became part of a cottage industry contributing to the supplies distributed by bootleggers. Even committed Prohibitionists appeared to believe that the public would not tolerate any effort to criminalize the act of drinking itself. The Volstead Act, unlike some state laws, permitted the manufacture of beer as long as the beer contained no more than 0.5 percent alcohol (near beer).

Patrons of a speakeasy enjoy their drinks, which were illegal under the Volstead Act. © BETTMANN/CORBIS.

EFFECTS OF PROHIBITION

Given the common belief that Prohibition failed to alter the consumption of alcohol or its adverse effects on health, it is appropriate to ask: To what extent did the law reduce alcohol use in the United States? First, there is no question that it succeeded in eliminating 170,000 saloons, even if it did not change the attitudes of most Americans about the morality of drinking. And, although some writers have asserted that drunkenness actually increased during Prohibition, most available records point to the opposite conclusion (Aaron & Musto, 1981; Lender & Martin, 1987). The most consistent findings on the impact of Prohibition come from statistics on medical problems linked to alcohol consumption, especially excessive alcohol consumption. Among these problems were hospital admissions for alcoholism and admissions to state mental institutions for alcoholic dementia and alcoholic psychosis. Striking decreases were observed in New York and Massachusetts, two states that did not have restrictions on alcohol consumption prior to 1920. Massachusetts state mental hospital admissions for alcoholic psychosis fell from 14.6 per 100,000 in 1910 to 6.4 in 1922 and were 7.7 in 1929; in New York, such admissions fell from 11.5 in 1910 to 3.0 in 1920, rising again to 6.5 in 1931 (Aaron & Musto, 1981).

Deaths from alcohol-related diseases also fell. National statistics showed that the number of deaths from cirrhosis (about 14.8 per 100,000 in 1907) were only 7.9 in 1919, 7.1 in 1920, and did



Bar graph showing gallons of alcohol consumed per capita during Prohibition, 1910–1929. ILLUSTRATION BY GEORGE BARILLE. GALE, CENGAGE LEARNING.

not rise above 7.5 during the 1920s. There were decreases in arrests for drunkenness and in costs of jailing public inebriates. Commander Evangeline Booth of the Salvation Army asserted that not only had drinking fallen off sharply, especially among the poor, but there were fewer broken homes because of wages lost to drinking or violence related to drinking.

Paul Aaron and David Musto state, "Observers . . . have been unanimous in concluding that the greatest decreases in consumption occurred in the working class . . . In large measure, intoxicants priced themselves out of the market" (Aaron & Musto, 1981, p. 165). A quart of beer and a quart of gin were each five to six times more expensive in 1930 than they were prior to Prohibition. Prohibition defenders asserted that instead of purchasing liquor in saloons, workers were putting their earnings into cars and refrigerators. Admittedly, the impact on alcohol consumption was greatest in the early years of Prohibition. As bootlegging increased in the late 1920s, medical problems linked to alcohol use rose again, but they did not reach the high levels experienced before 1920. Other data on per capita alcohol consumption immediately after repeal in 1934 indicated that there had been a drastic decline in average alcohol consumption during the Prohibition years.

BOOTLEGGING

Undoubtedly, crime associated with bootlegging increased. Many bootleggers became quite wealthy. Some who were involved in illegal activities prior to Prohibition used the wealth flowing from bootlegging to extend and further develop organized criminal enterprises, some of which later became involved with trafficking in illicit drugs. One of the most notorious figures associated with organized crime was Al Capone, who came to national attention because of his Chicago-based criminal activities. Aaron and Musto point out, however, that organized rackets existed in large cities before Prohibition and that the homicide rate increased most sharply between 1900 and 1910.

Unquestioned, also, is the unreliable quality of bootlegged liquor, much of which was produced by diverting or hijacking industrial alcohol. Some industrial alcohol could be flavored and sold as scotch, gin, or bourbon. Much of it, however, had been mixed with methanol (methyl alcohol) or other chemicals to render it undrinkable—denatured. Bootleggers hired chemists to remove the denaturants by redistillation (*washing*). Inadequate processing, which was not uncommon, produced a liquor that could be toxic or even lethal. The liquor produced in England and Canada and smuggled in

by ship or truck was of a higher quality. One smuggler who brought in such quality liquor, Bill McCoy, was responsible for the term still used to describe an authentic product—the "real McCoy."

CRITICISM OF PROHIBITION

The continued criticism of Prohibition and the frustration of enforcing the Volstead Act led many of its advocates to become increasingly defensive and hostile to non-supporters. Concern for the drunkard sharply diminished. According to Lender and Martin, "Many crusaders began labeling rehabilitation as nothing more than a waste of time and energy; prohibition, they promised would make such work unnecessary" (Lender & Martin, 1987). Groups interested in treatment declined. The Association for the Study of Inebriety dissolved in the mid-1920s. Volstead Act advocates became more hostile toward alcoholics as criticism of Prohibition increased. Some suggested amending the act to make drinking itself a criminal offense. One such suggestion came from an official in the Prohibition Unit of the Treasury Department, Harry J. Anslinger, then the Assistant Commissioner of Prohibition. Thus the 19th century concerns of the Temperance Movement for the physical and spiritual health of alcoholics turned, in the 1920s, to calls for stiffer jail terms, or even exile, for chronic alcoholics. In the context of these attitudes, the harsh penalties meted out under the leadership of the Treasury Department for mere possession of illicit drugs become somewhat more comprehensible.

The enforcement of the Volstead Act had been vested in the Treasury Department's Prohibition Unit within the Internal Revenue Bureau. The first National Prohibition Administrator and head of the Prohibition Unit was John F. Kramer. The Narcotics Division, headed by Levi G. Nutt, a pharmacist by training, was part of the Prohibition Unit. The Narcotics Division became an independent unit in the Treasury Department in 1930 when the Prohibition Unit was transferred to the Department of Justice. Harry J. Anslinger was appointed first Commissioner of Narcotics.

CHANGES TO THE VOLSTEAD ACT

Despite growing criticism, Prohibition, according to Aaron and Musto, was still alive and well when Herbert C. Hoover was elected president by a large margin in 1928. An overwhelming majority of both houses of Congress and nearly all the state governors supported the Eighteenth Amendment. Even opponents of Prohibition did not realistically expect to see it repealed. But the onset of the Great Depression in 1929 dramatically changed the situation. Opponents of Prohibition no longer argued for its repeal because of its demoralizing effects on civil liberty, but argued instead that the revival of the liquor industry would provide jobs and tax revenue. In the 1932 campaign for the presidency, Franklin D. Roosevelt promised to repeal Prohibition. Almost immediately after his inauguration, he introduced changes in the Volstead Act to legalize the sale of beer.

In 1933 the Twenty-first Amendment to the Constitution was ratified. It was brief and to the point: "Section 1. The Eighteenth Article of Amendment to the Constitution of the United States is hereby repealed." The federal government, however, retained responsibility to regulate and tax beverage alcohol and to prevent its illegal production. Section 2 of the Amendment allowed the states to continue Prohibition under state laws if they so desired. Some states did so; many states adopted alcohol beverage control laws (ABC laws) to curb the abuses that had characterized the production and sale of alcohol prior to prohibition. Among other provisions, ABC laws restricted the hours when alcohol could be sold (to make taverns and bars less attractive) and banned liquor sales on Sundays and election days. Some ABC laws created state-operated monopolies for the sale of packaged beverages. The federal laws dealing with control of alcohol remained the responsibility of various federal agencies. It was not until 1972 that they were brought together and responsibility for overseeing them was assigned to a single agency—the Bureau of Alcohol, Tobacco, and Firearms (BATF) in the Department of the Treasury.

Author Richard Hamm has observed that the Eighteenth Amendment had long-term consequences for American law and constitutionalism. The amendment both facilitated the growth of the law-enforcement establishment within the federal government, and it directly influenced the shape of the constitutional system "by specifying a seven-year time limit for ratification." Time limits such as this became the order

of the day, allowing the opponents of amendments "to translate delay into defeat" (Hamm, 2001, p. 218).

See also **Alcohol: History of Drinking in the United States; Temperance Movement; Woman's Christian Temperance Union.**

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PROPOXYPHENE. *d*-Propoxyphene (Darvon) is an opioid drug that is structurally related to methadone. It is used clinically to produce analgesia when the level of pain is not severe. Its popularity rests largely on the belief that propoxyphene is less likely to cause addiction than codeine, a drug that is also used for relief of moderate levels of pain. Propoxyphene is typically used in combination with aspirin or acetaminophen. Its analgesic effects are synergistic with those of aspirin and other nonsteroidal anti-inflammatory agents.

When it was introduced into clinical medicine in the early 1960s, propoxyphene was not subject to special narcotic regulatory control. This fact may explain its early popularity, which was probably due to clinicians' unrealistic fears about the addictive potential of codeine and to the inconvenience of prescribing it under the narcotic regulations that were in effect before the the Controlled Substances Act of 1970 was passed.

Although propoxyphene has only one-half to two-thirds the potency of codeine, it has been used to control symptoms of the opioid withdrawal syndrome. It is not commonly abused because it produces unpleasant toxic effects at high doses.

See also **Opiates/Opioids.**

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PSILOCYBIN. Psilocybin is an indole-type hallucinogen, found naturally with another hallucinogen in a variety of mushrooms—the most publicized being the Mexican or magic mushroom, *Psilocybe mexicana*, as well as other *Psilocybe* and *Conocybe*

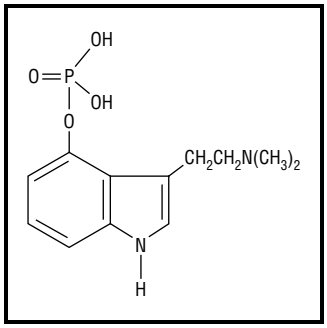

Figure 1. Chemical structure of psilocybin. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

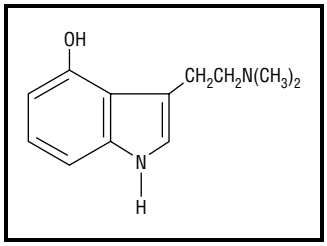

Figure 2. Chemical structure of psilocin. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

species. These mushrooms have long been consumed by Native Americans, especially in Mexico and the southwestern United States, as part of religious rites.

Psilocybin produces effects similar to lysergic acid diethylamide (LSD), but it is less potent and is metabolized in the body to form psilocin, another hallucinogenic compound. Both of these compounds have been synthesized in clandestine laboratories and made available on the streets.

See also **Hallucinogenic Plants; Peyote; Plants, Drugs From.**

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PSYCHIATRIC RESEARCH INTERVIEW FOR SUBSTANCE AND MENTAL DISORDERS (PRISM). *See* **PRISM.**

PSYCHOACTIVE. *Psychoactive* is a general term that came into use about 1961. It describes a substance that affects the central nervous system, producing changes in mental activity and/or behavior. A psychoactive substance or process may affect the way an individual thinks or the manner in which the environment is perceived or experienced; it may also change the behavior of an individual in a given situation.

See also **Psychopharmacology.**

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PSYCHOACTIVE DRUG. Any of a group of drugs (also called psychotropic drugs) that act upon the central nervous system, producing changes in mental activity and/or behavior. Psychoactive drugs are among the most widely used group of pharmacologically active agents, with extremely important clinical applications, including anesthesia for surgery and analgesia for relief of pain. They are also used for nonmedical purposes, such as to alter consciousness, improve performance, and as elements in cultural and religious rituals (alcohol and peyote are examples). Some psychoactive drugs produce an effect in those who suffer from a mental or medical disorder, but have no effect on normal individuals. The antidepressants, for example, have little or no effect on normal individuals other than side effects. Other psychoactive drugs, such as the sedative-hypnotics, produce effects in all individuals.

Psychoactive drugs are used to suppress disorders of movement and to treat anxiety disorders, depression, bipolar disorder (manic depression), and schizophrenia, among other mental illnesses. In addition, drugs used primarily to treat disorders in peripheral organs can also affect the central nervous system (e.g., beta-blocking agents, used to treat high blood pressure or disorders of heart rhythm; or steroid hormones, used to control inflammation). The psychoactive effects of these drugs are generally considered side effects, although some are used for their psychoactive properties as well.

Culturally approved nonmedical psychoactive drugs include alcohol, nicotine (tobacco), and caffeine. Psychoactive drugs that have been determined to have a high potential for harm and little medical benefit include heroin, hallucinogens, and some older sedative-hypnotics such as methaqualone. Marijuana has traditionally been placed in this category, but research has demonstrated potential effectiveness for medical problems including glaucoma, nausea, and weight loss associated with cancer or AIDS.

See also **Alcohol; Caffeine; Nicotine; Pain, Drugs Used for; Peyote; Sedative-Hypnotic; Tobacco.**

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PSYCHOANALYSIS. Psychoanalysis is an analytic technique originated by Sigmund Freud (1856–1939), an Austrian neurologist. It has been altered by his students and their students, in turn, throughout the twentieth century. Psychoanalysis is a theory of the way the mind works: (1) Sequences of thoughts are determined—they do not occur by chance; (2) Much of our thinking takes place out of awareness—it is unconscious and not easily recovered; (3) The experiences of early childhood, particularly those with important caretakers, continue to have an impact (often unconsciously) on our daily lives; (4) Feelings, both sexual and aggressive, are present at birth and affect behavior. Psychoanalytic theory helps us understand something of addicts' complex motivations and of their inner experiences and behaviors.

Psychoanalysis is also a method: It attempts to understand mental processes by free association (following thoughts wherever they lead without selection or censoring) and by the analysis of dreams, fantasies, and behaviors. Psychoanalysts apply this method as a therapy or treatment for certain forms of mental disability.

See also **Freud and Cocaine.**

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PSYCHOMOTOR EFFECTS OF ALCOHOL AND DRUGS. The psychomotor effects of alcohol and other drugs are costly. Thirty-nine percent of traffic fatalities are associated with alcohol. Twenty-five percent are associated with other drugs (Kaplan, Kraner, & Paulozzi, 2006, pp. 1293–1296). The majority of these fatalities can be linked to a driver under the influence. However, alcohol or drug use by pedestrians also contributes to the fatality statistics in a substantial manner.

PSYCHOMOTOR PERFORMANCE

Driving a car, crossing a street, or working on an assembly line are psychomotor tasks. Over many decades, researchers have examined the effects of drugs on the performance of these and other tasks or tasks that closely approximate them. Researchers have also examined drug effects on stimulus perception time, memory retrieval time, and other information processing activities that are commonly engaged by many tasks. Although the information provided by available research is already

extensive, the vast range of possible tasks, as well as the large number of available drugs, doses, and combinations means that research in this area must continue if our goal is to understand the impairing properties of alcohol and other drugs under all relevant circumstances.

Interpreting the psychomotor effects of a drug is complicated by a number of factors. The most obvious factor is the state of the subject when exposed to the drug. For example, some stimulant drugs, including caffeine and nicotine, will affect psychomotor performance only when the subject is sleep-deprived or fatigued but will have minimal effects at other times. In part this is simply a measurement issue: a subject who is already performing at his/her best has little room for improvement and will respond minimally to a performance-enhancing drug. Similarly, a subject performing at his/her worst will show minimal deterioration when confronted with a drug expected to impair performance. The individual's experience in performing the task and the degree to which the task can be performed with minimal (automatic) versus substantial cognitive effort will also determine whether task performance is drug sensitive.

In addition to these factors, variation in the response to a drug is related to traits (enduring characteristics) of the people under study. Some characteristics (e.g., genetic differences) may be unknown or unknowable and may produce different responses from one individual to the next. Other characteristics may be knowable but may confuse the interpretation of the results. For example, consider a study in which the research subjects are college students. Most college students have above-average intelligence, good problem solving skills, and no history of medical or psychiatric complications. As a result of their higher baseline function, they may be capable of exerting more cognitive effort or have the cognitive flexibility and motivation to adopt an alternate problem-solving strategy when a task becomes too difficult. Accordingly, when confronted with a drug challenge, they may show less performance impairment than subjects with less cognitive reserve.

A final example of a characteristic that can modify responsiveness is previous exposure to the drug. If the level of exposure is sufficient, then a neurophysiological adaptation may occur. This neuroadaptation is known as *tolerance*. Tolerance is indicated when repeated administrations of the same dose of the drug no longer evoke the same response and a higher dose than the original is required to reinstate the original response. Tolerance can be a powerful determinant of responsiveness. For example, police reports include many examples of alcohol-dependent drivers with blood alcohol levels sufficient to incapacitate or kill a nonalcoholic, and yet these individuals were capable of walking, talking, and driving before they were arrested.

ALCOHOL

The effects of alcohol obviously depend upon the dose and the rate of administration. Among nonalcoholics, blood-alcohol concentrations above the legal limit for driving, 80 mg/dL, depress many cognitive and motor skills. At lower concentrations, the effects of alcohol become task-dependent. Tasks that require the discrimination of one stimulus from another based upon simple visual (e.g., color) or auditory (e.g., pitch) cues are notoriously insensitive to alcohol concentrations below the legal limit, according to studies reviewed by Lance O. Bauer (2001). It is likewise true that tests of working memory or sustained vigilance are insensitive to the effects of an alcohol challenge unless the dose is large. Indeed, Tilman Schulte, Eva M. Müller-Oehring, Hans Strasburger, Hans Warzel, and Bernhard A. Sabel (2001) note that in many studies described in the literature over several decades, alcohol does not reliably impair performance when attention is focused on a single attribute.

In general, tests of divided attention and simulated driving are optimal for detecting the performance-impairing effects of alcohol (Liu & Fu, 2007; Moskowitz, Burns, & Williams, 1985; Ogden, & Moskowitz, 2004). In a dose-related manner, alcohol impairs visual search behavior during simulated driving; specifically, it increases fixation duration, decreases eye movements, slows saccade onset, and produces eye tremor (nystagmus) during visual tracking. It impairs steering accuracy and the maintenance of a constant following distance. Low doses of alcohol have also been shown to degrade performance on tasks that require inhibition of a powerful response tendency. A real world example of this impairment is failing to override the impulse to look at an interesting scene (e.g., a car crash) as one drives by.

A notable and obvious effect of alcohol is its ability to impair balance and gross motor skills (Goebel, Dunham, Rohrbaugh, Fischel, Stewart, & Hanson, 1995). Alcohol impairs balance and coordination in a dose-dependent manner: as the dose increases, the level of impairment increases proportionately.

Although many studies demonstrate adverse effects of alcohol on the performance of psychomotor tasks presented in a laboratory, caution is needed when generalizing results to settings outside of the laboratory. Yet, it remains possible that impaired performance on some laboratory tests would generalize. For example, one laboratory task affected by alcohol involves measuring accelerator pedal release time during simulated driving. Under specific circumstances, such as driving in heavy traffic, a slight delay in releasing the accelerator pedal and applying the brakes can cause an accident and bodily harm (e.g., a 0.2 second delay in applying the brakes at 65 mph increases the stopping distance by 19 feet). Under other circumstances, such as driving in light traffic, the increase in stopping distance would have no impact. Similar scenarios can be envisioned that enhance the danger associated with impaired balance/motor coordination (e.g., operating a motorcycle at higher speed) or divided attention (e.g., negotiating an exit from a busy parking lot after an athletic event while hundreds or thousands of other drivers exit the same parking lot). When contemplating findings from laboratory studies, one must be mindful that an intoxicated subject will not be at risk for accidents at all times under all circumstances. The threat to personal or public safety associated with alcohol may be constrained by individuals' specific occupations and activities. If a subject becomes intoxicated and is then confronted by a specific high-risk circumstance, then these otherwise minor psychomotor impairments may prove significant.

DRUG-ALCOHOL INTERACTIONS

Although many people believe that the adverse effects of alcohol can be antagonized, or reversed, by stimulant drugs, the evidence in support of this belief is remarkably weak. For example, although caffeine (Marczinski & Fillmore, 2003) and nicotine can, under some circumstances, successfully antagonize the slowing of reaction time caused by alcohol, they do not antagonize alcohol's adverse effects on executive control and balance/coordination or alcohol's propensity to increase risk taking. Beliefs regarding the psychomotor effects of caffeine or nicotine on alcohol intoxication can sometimes be a more powerful determinant than their actual effects, according to a 2002 study done by Mark T. Fillmore, Emily L. Roach, and Julietta T. Rice.

In the majority of cases, the use of alcohol and another drug together is more detrimental to performance than either drug administered alone. When doses are large, severe sedation or loss of consciousness may result, leading to obvious impairment in task performance. When doses are in the small-to-moderate range, interactions are detectable and occasionally specific to a certain task or skill.

ALCOHOL AND BENZODIAZEPINES

When taken at the proper dosage, benzodiazepines have a low potential for acute toxicity. However, when taken with alcohol (ethanol), their sedative properties can be magnified (Simpson & Rush, 2002) and may pose a serious medical risk. Taken together, benzodiazepines and alcohol increase the perception of drunkenness and impair balance and cognitive flexibility more than when either drug is taken alone. A notable and profound effect of the drug combination is its ability to impair learning and memory. Benzodiazepines, in particular, cause state-dependent learning—an impairment wherein information acquired in the intoxicated state is less easily recalled in the sober state (or vice-versa). This is one reason that benzodiazepines are commonly administered during surgical procedures.

ALCOHOL AND CANNABIS

The acute effects of cannabis (marijuana) on psychomotor performance are modest. Apart from its documented ability to impair short-term memory and recognition/recall performance, low doses of cannabis have negligible effects on reaction time in simple and complex settings. Although cannabis is detrimental to psychomotor performance at higher doses, its effects remain less profound than those of alcohol and some other drugs. Furthermore, it appears that cannabis affects a different set of performance skills than those affected by alcohol.

ALCOHOL AND OPIATES

The acute effects of opiates on psychomotor performance have not been studied extensively. The

most notable and reproducible decrement is an impaired ability to perceive and discriminate visual stimuli. This decrement might be wholly attributable to pupillary constriction and blurred vision. Yet, Zacny, Conley, and Galinkin (1997) have shown that it may reflect a central reduction in attention and in the ability to accurately perceive and encode stimuli in any modality, visual or otherwise. Greater performance declines have been reported following buprenorphine than morphine.

Opiates produce sedation. They can thereby impair the ability to maintain alertness during long vigils, such as driving along a highway for an extended distance. These adverse effects can combine with the sedative effects of alcohol or sleep deprivation to increase risk for performance failures (e.g., motor vehicle accidents).

See also **Accidents and Injuries from Alcohol; Accidents and Injuries from Drugs; Antagonists of Alcohol and Drugs; Benzodiazepines; Blood Alcohol Concentration; Driving, Alcohol, and Drugs; Drug Interactions and Alcohol; Marijuana (Cannabis); Memory, Effects of Drugs on; Opiates/Opioids; Productivity: Effects of Alcohol on.**

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PSYCHOMOTOR STIMULANT. This term is used to describe drugs that act as central nervous system (CNS) stimulants. Such drugs generally are appetite suppressants, decrease sleep and fatigue, increase energy and activity, and at higher doses can cause convulsions and death.

Ingestion typically results in increased wakefulness and a decreased sense of fatigue; increased speech and motor activity; alertness; and frequently elevation of mood. Many of the drugs in this class have a potential for abuse, with reports of euphoria at higher doses. Although users often report improved performance on physical and mental tasks, this is rarely the case, but they do restore performance that has been impaired by fatigue.

Prolonged use of most of these drugs can result in tolerance to many of their effects. Repeated high doses can result in distorted perception and overt psychotic behavior.

See also **Amphetamine; Cocaine; Tolerance and Physical Dependence.**

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PSYCHOPHARMACOLOGY. Psychopharmacology is that branch of science that involves the study of the effects of interactions between drugs that affect the central nervous system (i.e., psychoactive drugs) and living systems. Behavioral and neurobiological effects as well as the mechanisms of actions and side effects of drugs are often examined. Preclinical studies of psychoactive drugs using animal models and tissue preparations are an important aspect of psychopharmacology, contributing to our understanding of the mechanisms involved in disorders of the central nervous system and mental illness. Clinical psychopharmacological investigations include examining the effects of drugs used in treating psychiatric disorders (such as anxiety, depression, schizophrenia, and mania), as well as other dysfunctions within the central nervous system (such as movement disorders, Alzheimer's disease). Also included is study of the effects of psychoactive drugs used nonmedically to induce altered states of consciousness, to improve mood, or to otherwise affect the mental status and/or behavior of the individual. A growing area of research in psychopharmacology addresses disorders of addiction or dependence to some of these drugs. New treatments for alcoholism (naltrexone), opioid dependence (buprenorphine), and smoking cessation (bupropion) have resulted from these efforts, and many more treatments are under development. Some of the drugs used for treatment of depression and anxiety are also being investigated for potential usefulness in treating substance dependence, since it is often accompanied by these comorbid conditions.

Psychopharmacology is an interdisciplinary field of science. Psychopharmacologists may be physicians trained in psychiatry or neurology; psychologists with extra training in pharmacology; or pharmacologists with special training in psychology and behavior.

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PUBLIC INTOXICATION. In 1606 England first made simple public intoxication a criminal offense. This English precedent was reflected in laws in the American colonies as well as in city, county, and state laws enacted after the American Revolution. By the early 1960s about 2 million arrests occurred annually for simple public intoxication, representing about 33 percent of all arrests in the United States.

Since then, changes have occurred in the handling of public intoxication. Through initial efforts in the judicial/court system and later through federal and state legislation, the handling of public intoxication was transferred from the criminal-justice system to the more humane and effective public-health care system. Major obstacles to further progress, however, have been the lack of adequate funding and the struggle to find effective alcohol abuse and alcoholism treatments.

INITIAL COURT CHALLENGES

Beginning in 1964, lawyers argued that alcoholics could not lawfully be punished for public intoxication. First, they argued that alcoholics did not have the *mens rea* (Latin, guilty mind or intent) required for conviction of a crime, because public intoxication was a symptom of the disease of alcoholism. Second, they argued that punishing an alcoholic for exhibiting symptoms of a disease was cruel and unusual punishment, prohibited by the U.S. Constitution.

In lower court cases these arguments prevailed. In 1968, however, in the case of *Powell v. Texas*,

the U.S. Supreme Court handed down a split decision on this issue. Four justices deemed it cruel and unusual punishment to convict Powell, an admitted alcoholic, for public intoxication. Four others determined that the matter should be decided on a state rather than a constitutional level. The ninth and controlling justice said that, because Powell had a home, he could properly be held responsible for being intoxicated in public, so he was convicted. This opened the question of whether a homeless alcoholic could also be convicted.

In response to the costs of transporting and detaining public inebriates, some communities have instituted "sobering centers" where intoxicated individuals can safely spend the night and receive treatment referrals. AP IMAGES

ENACTMENT OF FEDERAL STATUTES

Faced with a stalemate in the Supreme Court, advocates for reforming public-intoxication laws turned to Congress. In spite of a large number of federal public health statutes, none referred explicitly to the problems of intoxication and alcoholism. Congress responded by enacting the Alcoholic Rehabilitation Act of 1968, which recognized alcoholism as a major health and social problem and recommended handling public intoxication as a health problem rather than a law-enforcement matter. The Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment, and Rehabilitation Act of 1970 (also called the Hughes Act) followed. It created the National Institute on Alcohol Abuse and Alcoholism to administer all alcoholism programs under the authority of the U.S. Department of Health, Education, and Welfare (now the U.S. Department of Health and Human Services). These new federal laws for the first time provided a national focus for handling intoxication on a public-health basis.

CHANGES IN STATE STATUTES

Following the legal developments in the courts and in Congress, state and local laws rapidly changed. Initially in the District of Columbia and in Maryland, and subsequently throughout other parts of the country, criminal statutes prohibiting simple public intoxication were repealed and replaced with new laws establishing detoxification programs for intoxicated persons and rehabilitation programs for chronic alcoholics.

Federal and state laws now provided a firm foundation for handling public intoxication as a public-health problem rather than as a matter for the criminal-justice system. Relatively little additional change could be accomplished solely by further litigation or legislation, but two additional obstacles arose. First, the competition for federal and state health funds became intense. Other important health needs, including basic health care for the needy and treatment for people with acquired immunodeficiency syndrome (AIDS), made it difficult for public officials to devote adequate resources to expanding public-health programs for alcoholism. The problem was compounded by uncertainty as to the best method for preventing or treating intoxication and alcoholism. A low rate of rehabilitation led many public health officials to conclude that scarce public resources could be more effectively devoted to other illnesses, especially communicable diseases. Without additional investment, the police remain deeply involved in identifying and responding to intoxicated individuals, and their response is not necessarily limited to transporting individuals to sobering-up stations.

Progress in the prevention and treatment of intoxication and alcoholism has therefore been slow. Unless and until the American public places a higher priority on public intoxication as a public-health matter or medical science finds more effective methods to prevent and treat this problem, this situation is unlikely to change.

Two developments in the last decade of the twentieth century illustrate the public concern and frustration with the continuing problems of

public intoxication and alcoholism. First, publicity about the substantial death and destruction caused by people driving under the influence of alcohol has led to more stringent penalties and stricter enforcement against this behavior. Second, tragic deaths caused by binge drinking on college campuses have led to an increase in the drinking age from 18 to 21 as well as stricter enforcement in college towns throughout the country.

CHRONIC PUBLIC INEBRIATION (CPI) AND SOBERING CENTERS

In the absence of an optimal treatment and prevention program or unlimited funds to administer such a system, individuals will continue to become intoxicated; some will be termed chronic public inebriates (CPI). To keep down the staggering costs of emergency department or law enforcement personnel transporting intoxicated individuals to detention facilities for sobering up, many states have created *sobering centers*. These nonmedical, non-detention centers allow intoxicated persons to safely spend the night (or other brief interval). They also provide food, showers, and referrals to treatment or rehabilitation facilities. Individuals can stay the night to sleep off the effects of alcohol, or they can stay for several days to engage in assessment and programming activities. In many sobering centers, clients are encouraged to attend self-help or twelve-step meetings and to consider referral to longer-term treatment facilities. Typically, sobering centers are based on the philosophy that many alcoholics also have mental health disorders (co-occurring disorders), so they offer screening and referral for behavioral health (mental health and substance abuse) problems. Many sobering centers offer intensive case management services, housing referrals, and other public assistance along with detoxification and assessment protocols.

See also **Alcohol: History of Drinking; Homelessness, Alcohol and Other Drugs, History of; Temperance Movement; Treatment, Stages/Phases of: Non-Medical Detoxification; Treatment, Stages/Phases of: Medical Detoxification; Treatment: An Overview of Alcohol Abuse/Dependence; Treatment: A History of Treatment in the United States.**

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RACIAL PROFILING. Profiles, formal and informal, are common in law enforcement, particularly in narcotics law enforcement. They consist of general characteristics, features, and behaviors that might make a law enforcement officer suspicious. In some instances, law enforcement agencies formulate and disseminate formal profiles to officers to guide their investigative actions. Even when profiles are not formally maintained, however, officers inevitably rely on their past experience to generate informal profiles to help them determine who to follow more closely, approach, stop, or question. There is much controversy regarding profiling as a general practice. When race becomes a factor in a profile, however, serious constitutional and ethical issues arise.

STATISTICS ON RACIAL TARGETING

Racial profiling is the use of racial of ethnic generalizations or stereotypes as a basis for stopping, searching, questioning, or detaining an individual. Racial profiling has received a great deal of attention in the United States, beginning in the late 1990s with a series of prominent incidents and the release of data on police practices from several jurisdictions. The data consistently showed that African Americans and Hispanics are disproportionately targeted by law enforcement for stops, frisks, and searches. Court records showed, for example, that in Maryland African Americans made up 70 percent of those stopped and searched by the Maryland State Police from January 1995 through December 1997, on a road on which 17.5 percent of the drivers and speeders were African American. A 1999 report by the New Jersey attorney general found that 77 percent of those stopped and searched on New Jersey highways were African American or Hispanic, even though, according to one expert, only 13.5 percent of the drivers and 15 percent of the speeders on those highways are African American or Hispanic.

An *Orlando Sentinel* analysis of 1,000 videotapes of Florida state trooper traffic stops in 1992 showed that on a road where 5 percent of the drivers were African American or Hispanic, 70 percent of those stopped and 80 percent of those searched by the Florida state police were African American or Hispanic. Although matters had improved somewhat by the start of the twenty-first century in terms of racial percentages at traffic stops, there has been little change in what occurs *after* the initial stop. According to Bureau of Justice statistics, Blacks, Hispanics and Whites are pulled over with roughly equal frequency, but Blacks and Hispanics are far more likely to be questioned, searched, handcuffed, detained, or arrested than their White peers. For every three White people subjected to more than a simple traffic stop, at least 10 Blacks and 11 Hispanics were searched.

Racial targeting need not be expressly invited by a profile. Consider, for example, the U.S. Drug Enforcement Agency's (DEA) drug courier profile for airports. All the factors listed below have been identified by DEA agents in court testimony as part of the DEA's drug courier profile:

- Arrived late at night.
- Arrived early in the morning.
- Arrived in afternoon.

- One of first to deplane.
- One of last to deplane.
- Deplaned in the middle.
- Bought coach ticket.
- Bought first-class ticket.
- Used one-way ticket.
- Used round-trip ticket.
- Paid for ticket with small denomination currency.
- Paid for ticket with large denomination currency.
- Made local telephone call after deplaning.
- Made long-distance telephone call after deplaning.
- Pretended to make telephone call.
- Traveled from New York to Los Angeles.
- Traveled to Houston.
- Traveled to Detroit.
- Traveled to Miami.
- Carried no luggage.
- Carried brand-new luggage.
- Carried a small bag.
- Carried a medium-sized bag.
- Carried two bulky garment bags.
- Carried two heavy suitcases.
- Carried four pieces of luggage.
- Overly protective of luggage.
- Disassociated self from luggage.
- Traveled alone.
- Traveled with a companion.
- Acted too nervous.
- Acted too calm.
- Made eye contact with officer.
- Avoided making eye contact with officer.
- Wore expensive clothing and gold jewelry.
- Dressed casually.
- Went to restroom after deplaning.
- Walked quickly through airport.
- Walked slowly through airport.
- Walked aimlessly through airport.
- Left airport by taxi.
- Left airport by limousine.
- Left airport by private car.
- Left airport by hotel courtesy van.
- Suspect was Hispanic.
- Suspect was African American female.

Even without the last two factors, this profile describes so many travelers that it does not so much focus an investigation as provide DEA officials a ready-made excuse for stopping whomever they please. The profile for terrorists is quite similar, with the addition of *Muslim* as a race/ethnicity.

Although statistical data alone do not conclusively establish that officers are engaged in racial profiling, they provide strong circumstantial evidence. Many police officers, moreover, admit that all other things being equal, they are more suspicious of, for example, young African American men than elderly White women. Nor is such thinking irrational. Criminologists generally agree that young (African American) men are more likely to commit crime than elderly (White) women, because at least with respect to some crime, young people commit more crime than old people, men commit more crime than women, and African Americans commit more crime than Whites. Indeed, it is precisely because the use of race as a generalization is not irrational that racial profiling is such a widespread phenomenon.

USE IN DRUG LAW ENFORCEMENT

In some areas, however, there is evidence that the use of racial profiles is irrational. The strongest evidence is with respect to drug law enforcement. Much of the racial profiling that occurs on the nation's highways is conducted for drug law enforcement purposes. Officers use the pretext of a traffic infraction to stop a car and then ask for consent to search the car for drugs. The U.S. Supreme Court has expressly approved this tactic.

Yet studies show that officers get virtually the same "hit rates" for Whites and African Americans when they conduct traffic stops for drugs. In other words, officers are no more likely to find drugs on an African American driver than a White driver. Consistent with these results, the U.S. Public Health Service has found, based on confidential self-report surveys, that African Americans and Whites use illegal drugs in rough proportion to their representation in the population at large. Because most users report having purchased drugs from a dealer of the same race, drug dealing is also likely to be fairly evenly represented demographically. Thus, the supposition that African

Americans are more likely to be carrying drugs is sharply contradicted by the data.

UNLAWFUL AND UNWISE

In any event, even where demographic data suggests that the practice of racial profiling may not be irrational, it is both unconstitutional and unwise. Because of the pernicious history of racial classifications in the United States, the Supreme Court forbids official reliance on racial generalizations—even accurate ones—except when there is no other way to achieve a compelling government end. The usual argument police officers advance in defense of profiling is that it recognizes the unfortunate fact that minorities are more likely than nonminorities to commit crime. Although this may be true with respect to *some* crimes, however, the generalizations are significantly overinclusive, even where those crimes are concerned. The fact that African Americans are more likely than Whites to engage in violent crime, for example, does not mean that most African Americans commit violent crime. Most African Americans, like most Whites, do not commit any crime; annually, at least 90 percent of African Americans are not arrested for anything. On any given day, the number of innocent African Americans is even higher. In addition, when officers focus on minorities, they lose sight of White criminals. Race is a grossly inaccurate indicator of crime.

Most important, relying on race as a factor for suspicion violates the first principle of criminal law: individual responsibility. The state's authority to take its citizens' liberty—and in extreme cases, lives—turns on the premise that all are equal before the law. Racial generalizations fail to treat people as individuals. As a result, policies that tolerate racial profiling undermine the criminal law's legitimacy. As any good leader knows, and many criminologists have confirmed, legitimacy is central to getting people to follow the rules. If people believe in the legitimacy and fairness of the system, they are much more likely to abide by the rules than if they see the system as unjust. Thus, racial profiling may indeed contribute to crime by corroding the legitimacy of the criminal law.

TERRORISM AND NEW RACIAL PROFILING

The terrorist attacks on American soil on 9/11, along with the attacks on Spain's railway system and the London transportation system, effectively reversed the antiprofiling trend. It added another group to be profiled, potential terrorists, and another racial/ethnic group to scrutinize: young Middle Eastern or Muslim-appearing males.

In addition to the ethical dilemmas inherent in search and seizure based on statistically determined racial or ethnic profiles is the logic flaw sharply exemplified by the twenty-first-century terrorist attacks: The persons who committed the violence were able to blend into the cultures in which they operated before their final acts. They didn't look substantially different than those around them, and they moved comfortably within the societies they targeted, whether in the United States, Spain, or the United Kingdom. Ethnic identity, or the appearance thereof, can be changed. In London, the members of the jihad cell shifted their assumed identities to East African to avoid being profiled as Pakistani or Arab.

Thus far, there is no convincing, empirical evidence that racial or ethnic profiling achieves the desired ends: eradicating crime or preventing acts of terror. When groups become aware that they are being profiled, they shift identities to assimilate (persons of African descent transform themselves into Jamaicans or Caribbeans, Mexicans become Spaniards, persons from the Middle East become African, etc.). When metal detectors were installed in airports a few decades ago, terrorists shifted from metal weapons to liquid and plastic explosives. Hijackings decreased, but bombings increased dramatically. These are called substitution effects.

Most counterterrorists are convinced that the way to combat terrorism is to effectively limit terrorist resources through the use of proactive counterterrorism activities and through the use of intelligence (informational resources). General Mier Dagan, the former head of the Bureau of Counterterrorism in the Office of the Prime Minister of Israel stated, "Investments in intelligence are invisible, whereas increased security is visible but often wasteful. The first priority must be placed on intelligence, then on counterterrorism operations, and finally on defense and protection."

See also **African Americans, Ethnic and Cultural Factors Relevant to Treatment for; Crime and Drugs; Driving Under the Influence (DUI); Hispanic Americans, Alcohol and Drug Use Among.**

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RAVE. Raves in the United States in the twenty-first century are similar in nature to those that emerged in the 1980s: Large parties held into the early hours of the morning characterized by loud electronic music, people socializing and dancing, and widespread substance use. While raves started out as *underground* parties held in clandestine locations known to the few, *raving* generally morphed into *clubbing*, which often occurs in legitimate, regulated venues attended by many people across the nation every weekend (Sanders, 2006; Hobbs et al., 2003; Thornton, 1995). No doubt underground raves still exist, and occasional super parties held in stadiums, convention centers, and open fields are billed and thought of as *raves* or *festivals*, but socializing to electronic dance music in semi-public venues while using one of a number of substances has become commonplace, another option within the leisure spectrum of many U.S. cities (Sanders, 2006; Presdee, 2000; Rojeck, 2000).

Underground raves and those who attend them are differentiated from *mainstream* club scenes and clubbers in terms of style, culture, musical preference, and other characteristics, but raving, festivals, clubbing, and the like in the early twenty-first century are, in the main, fundamentally commercial enterprises (Sanders, 2006; Thornton, 1995). This entry describes common forms of clubbing or raving, all of which is henceforth referred to as electronic dance parties (EDPs), so as not to confuse them with underground raves.

CLUB DRUGS AND THEIR USERS

To be sure, not all those who attend EDPs use drugs (National Institute on Drug Abuse, 2006). Certain types of drugs, collectively known as *club drugs*,

however, are commonly used at EDPs (Fendrich & Johnson, 2005). The drug ecstasy, which is often associated with MDMA (3,4-methylenedioxy-N-methylamphetamine), in particular, has been considered ubiquitous at EDPs (Beck & Rosenbaum, 1994; Sanders, 2006; Colin & Godfrey, 1997; Redhead, 1993; Shapiro, 1999). The drug, in a similar vein to other so-called club drugs—magic (psilocybin) mushrooms, and LSD (acid)—*fit* with the music and overall theme of the events (Sanders, 2006). The pulse of the beat, with names like *jungle*, *trance*, *hard house*, and *drum and bass*, work with the stimulant and hallucinatory effects of these drugs and are thought to enhance the visual effects of the lasers, disco balls, and general party atmosphere created by the venue and its punters (Reynolds, 1997). Other club drugs, such as ketamine (Special K), a *dissociative* anesthetic widely used in veterinary practices, and GHB, a simple carbohydrate which has been used by bodybuilders as a supplement, are also associated with EDPs (National Institute on Drug Abuse, 2006; Lankenau, 2006). Even the potent sedative, Rohypnol, was considered a club drug at one point (Maxwell, 2005). The uses of drugs such as powder cocaine and crystal methamphetamine (crystal) are, however, not uncommon at EDPs (Green, 2006; Kelly & Parsons, 2006; Kelly, Parsons & Brooke, 2006). Other powerful hallucinogens, known as tryptamines (DMT) and phenethylamines (2C-B), have also been reported at EDPs (Kelly, 2006; Sanders, 2006; Sanders et al., 2008). Again, both stimulants and hallucinogens work with the overall atmosphere produced at EDPs. If *club drugs* are those drugs used within such venues, then other substances fall in this category.

Individuals who use drugs are thought of *marijuana users*, *heroin users*, *ecstasy users*, and the like. These terms may capture particular drug consumption patterns. However, at EDPs, many individuals use multiple drugs, either sequentially or simultaneously (Lankenau & Clatts, 2005; Kelly, Parsons, & Wells, 2006; Klein, Sterk, & Elifson, 2006; Sanders, 2006). People attending EDPs are likely to use several substances over the course of the event, as opposed to sticking with one. Moreover, alcohol is prominent since many EDPs are held in venues that sell alcohol (Measham & Brain, 2005). The following example certainly does not apply to all who attend EDPs, but it does provide some insight into the potential for using a variety of substances while attending an event.

This example is derived from a slightly altered amalgamation of several ethnographic accounts of drug consumption at EDPs in the United States (Green, 2006; Navarez, 2001; Perrone, 2006). Friends meet up at a bar around 10 p.m. for a couple drinks. An hour later, they go to an EDP. Prior to entering the venue, they smoke a little cannabis. They enter the EDP buzzing from the alcohol and cannabis mixture. Around 12:30, they decide to take an ecstasy pill. Alcohol is sold in the venue, and these individuals decide to have a few drinks during their three-hour ecstasy high. At 3:30 a.m., their ecstasy buzz is wearing off, but the party does not stop for another couple of hours. Fortunately, they brought cocaine and crystal with them, and each sniffs a small amount of *trail mix*, a combination of both drugs. The trail mix keeps them going until 7 a.m., and when the party stops, they rally to a friend's house for a *chillout* session. To help them *comedown* from the ecstasy, cocaine, and crystal, they smoke some more cannabis, and have a few drinks. Despite the alcohol and strong, hydroponically grown cannabis, the trail mix keeps them going for a bit longer than expected. As a remedy, each takes a Vicodin prior to going to bed sometime in the late morning, 12 hours after they first headed out.

EDP ATTENDEES AND THEIR RISK OF LEGAL PROBLEMS

Individuals who attend EDPs are part of the workforce and attend EDPs in order to release tension and stress after a week's work (Green, 2006; Perrone, 2006; Sanders, 2006). These youth, in the main, lead normal, productive lives. Youth who attend EDPs en masse are not outlaws, not drug-crazed addicts, and evidence generally does not indicate that such individuals are more prone to crime and delinquency than their non-attending EDP counterparts (Sanders, 2006). To be clear, many punters may be chemically addicted and/or suffer from serious health problems related to their substance use, and accounts of overdose or drug-related negative health outcomes or death do occur at or around EDPs. But substance use consumption patterns among punters at EDPs appear largely recreational, and the youth who attend these events, in the main, have meaningful lives (Green, 2006; Perrone, 2006). These youth have generally not opted out of society and are not the

double failures as drug users were described generations ago (Cloward & Ohlin, 1960; Merton, 1957). Attendees at EDPs may be considered part of a broadly defined *subculture* to the extent that they enjoy similar forms of music, have a tolerance for drug use, and like to socialize during the early morning hours. However, beyond these preferences, such youth are remarkably different from one another and do not constitute a segment of the population otherwise distinct from everyone else (Presdee, 2000; Rojeck, 2000; Sanders, 2006; Thornton, 1995).

Criminal justice and public health reactions to EDPs are at odds with one another: The former seeks to curtail drug use at EDPs through sanctions and prosecution, whereas the latter attempts to make substance use safer for the evening's punters (Sanders, 2006). Dancesafe, for instance, is an organization largely run by those who enjoy EDPs. Dancesafe has offered pill-testing services by providing punters with testing kits in order to have their ecstasy tablets checked for content. Among other activities, Dancesafe has set up small booths in or around EDPs in order to provide information about drugs commonly used within such venues. While pill testing may be "harm minimization gone too far" (Winstock, Wolf, & Ramsey, 2005), it represents a unique public health approach towards reducing the potential of adverse affects related to recreational youthful substance use.

The contrast there is opposition to illicit substance use at EDPs. In 2002, for instance, the R.A.V.E Act was introduced (R.A.V.E stood for Reducing Americans' Vulnerability to Ecstasy). The act would make it illegal to use illicit drugs on venue premises, and if anyone was caught doing so, the owner and manager of the venue, and the night's promoters, as well as the offending punter, could all be subject to criminal prosecution. While the RAVE Act was never passed, its central tenets were incorporated into another bill—the Illicit Drug Anti-Proliferation Act of 2003—that eventually became law. The difficulty is in effectively policing this law (Measham, Alrdridge, & Parker, 2001). If EDPs are subject to closure as a consequence of one punter using illicit drugs inside the venue, then EDPs are surely doomed. Substance use—whether illicit or not—is common at most EDPs and may be seen as *normalized* within such settings (Measham et al., 2001). Shutting down illicit substance use at EDPs threatens their existence. This, in turn, not only jeopardizes a multimillion-dollar-a-year industry but may also serve to push EDPs further underground, away from regulated nightclubs and venues. If this occurs, then punters may become unnecessarily exposed to the public health hazards of clandestine EDP locations (Sanders, 2006).

The future of EDPs in the United States is not known. Youth at EDPs are exposed to a broad range of illicit substances, and, regardless of whether they decide to use them or not, most wake up the following morning and get on with their (largely) law-abiding lives. Substance-using youth may get caught in the legal system, which, in turn, can detrimentally affect the remainder of their lives. If attending EDPs and using drugs may be part of a fad or fashion that many youth pass through, then people need to think carefully about their responses to these criminal aspects of their otherwise productive, respectable and obedient young lives.

See also **Club Drugs; Cocaine; Lysergic Acid Diethylamide (LSD) and Psychedelics; Marijuana (Cannabis); MDMA; Media; Methamphetamine; Music; Psilocybin; Rohypnol.**

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BILL SANDERS

RECEPTOR, DRUG. A receptor is a molecular site, specific for a drug or its class, with which the drug must combine to produce its effect. If a drug is in the body but cannot bind to the receptor, then there is no effect. A receptor can be thought of as the button or switch that the drug must activate in order to produce a physiologic effect.

Receptors for drugs are the same receptors used in the brain by naturally occurring compounds called neurotransmitters. Neurotransmitters are chemical signaling messengers in the brain that work by

binding to specific receptors; a wide variety of drugs of abuse bind to these same receptors. In this sense, drugs of abuse insert themselves into natural and normal systems found in the brain and take over normal pathways in abnormal ways. Receptors are essential for normal functioning of the body and are therefore of great interest and importance in physiology and medicine.

Receptors can be stimulated by compounds called agonists, or blocked by compounds called antagonists. Antagonists prevent the action of agonists. For example, naltrexone, an antagonist, will prevent morphine, an agonist, from having any effect.

A major achievement of research in drug abuse over the past thirty years has been the identification and study of almost all receptors for drugs of abuse. Receptors are generally classified into two types: an ion channel type and a coupled type receptor or "G protein." Nicotine acts at one of the former and morphine at one of the latter. However, sometimes the initial molecular site where a drug acts is not one of these two classical types of receptors. For example, cocaine acts at another kind of molecule called a transporter for dopamine; after cocaine binds at this site, dopamine transport in the brain is blocked, which then results in increased actions at the dopamine receptor. Since receptors are the initial molecular sites of binding of drugs, they are clearly of interest in understanding how drugs produce their effects and how we might develop medications to treat drug abuse.

See also **Agonist; Agonist-Antagonist (Mixed); Neurotransmitters.**

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RECEPTOR: NMDA (N-METHYL D-ASPARTIC ACID). The NMDA receptor is a protein on the surface of neurons (nerve cells). When the major excitatory neurotransmitter, glutamate, binds to this protein, the central pore of the NMDA receptor channel opens—then cations (the ions of sodium, potassium, and calcium) are able to cross the cell membrane. The movement of cations through the pore results in neuronal excitation.

The NMDA receptor is one of several cell receptor surface proteins activated by glutamate. The hallucinogen phencyclidine (PCP) blocks the open channel of the NMDA receptor, preventing cation flow. It is believed that overactivation of the NMDA receptor could be responsible for the neuronal cell death observed following some forms of stroke; it may even be involved in the cell death associated with neurodegenerative diseases.

See also **Neurotransmission; Receptor, Drug.**

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RECEPTOR ANTAGONIST. *See* **Antagonist; Antagonists of Alcohol and Drugs.**

REINFORCEMENT. Although the term reinforcement has many common uses and associated meanings, its meaning is precise when used by behavior analysts and behavior therapists. The act or process of making a reinforcer contingent on behavior is termed positive reinforcement. A reinforcer is any object or event that, when delivered following some behavior, increases the probability that the behavior will occur again. A typical example might be observed in a laboratory experiment with rats. A rat is placed in a small plastic chamber. The rat can press a lever located on one

wall of the chamber. When the rat presses the lever, a small food pellet drops into a dish. If the rat returns to the lever and continues to press it would be said that the food pellet functions as a reinforcer and that the behavior is maintained by positive reinforcement.

There is often confusion between positive reinforcement and negative reinforcement. Negative reinforcement occurs when a behavior results in terminating an aversive stimulus. In the case of the rat, the negative stimulus might be a loud noise. A lever press turns off the stimulus. If the rat continues to press the lever, it would be said that loud noise functions as a negative reinforcer and the behavior is maintained by negative reinforcement. Thus, both positive and negative reinforcement refer to increases in behavior, but differ in whether a pleasant stimulus is presented as the result of some behavior (positive reinforcement). Negative reinforcement is also referred to as escape (if the response turns off the stimulus each time it appears) or avoidance (if the response can postpone presentation of the stimulus).

It is important to note that reinforcement is a concept that refers to the relationship between behavior and its consequences. Stimuli or events are not assumed to have inherent reinforcing effects. For example, although most people like money and will continue to exhibit behavior that results in obtaining money, it cannot be assumed that money functions as a reinforcer for everyone. For example, money might not serve as a reinforcer for a monk devoted to an ascetic lifestyle. The defining characteristic of reinforcement depends on how a behavior is changed and not on the types of things that serve as reinforcing events (Morse & Kelleher, 1977). Factors that help determine whether a given object or event is reinforcing or punishing for a given individual include that individual's previous experiences and other features of the environment that coexist and are associated with the object or event. The upshot is that different things may function as reinforcers for different people.

Drugs can serve as reinforcers that maintain drug-seeking and drug-taking behaviors. This fact can be observed in the prevalence of drug use among humans and has also been shown in laboratory research with animals. In a typical laboratory experiment, an animal such as a rat or monkey has a catheter placed in a vein and connected to a pump-driven syringe. The animal can press a lever to activate the pump, and this results in a dose of a drug such as cocaine, heroin, nicotine, or alcohol being infused into the vein. If the animal continues to press the lever to obtain the drug, then the drug is said to serve as a reinforcer. Interestingly, those drugs which lead to addiction in humans also serve as reinforcers in animals. The only exception is marijuana (THC), which is used fairly extensively by humans but does not function as a reinforcer in animals. It should be noted that drugs that serve as reinforcers under one condition may not serve as reinforcers under other conditions. For example, nicotine serves as a reinforcer only at low doses and when doses are properly spaced. Nevertheless, the observation that drugs of abuse generally function as reinforcers in experimental animals has brought the study of drug-seeking behavior and drug abuse into a framework that allows carefully controlled behavioral analyses and the application of well-established and objective behavioral principles (Schuster & Johanson, 1981).

The acquisition of drug use in humans predominantly involves positive reinforcement, whereas the maintenance of drug use can involve both positive and negative reinforcement. The ability of a drug to serve as a positive reinforcer is usually associated with its pleasurable subjective effects (e.g. a "rush," a "high," or other feelings of intoxication). But again, given the definition of reinforcement, it is not necessary for a drug to be subjectively reinforcing or pleasurable in order for it to maintain behavior. Many drugs are also associated with symptoms of withdrawal when abstinence is initiated following a period of regular use. In this case, taking the drug again may terminate the aversive state of withdrawal; in this way, drug use is maintained by negative reinforcement. Drug use can also be influenced by sources of reinforcement other than the direct effects of the drug. For example, social encouragement and praise from a peer group can play an important role in the development of drug use by teenagers. Biological factors may also come into play. For example, some individuals may be more or less susceptible than others to feeling and recognizing the pleasurable effects of drugs. When drug use is viewed as a behavior maintained by the reinforcing effects of

drugs, it suggests that this behavior is not amoral or uncontrolled but rather that it is the result of normal behavioral processes.

See also **Addiction: Concepts and Definitions; Research, Animal Model: An Overview; Risk Factors for Substance Use, Abuse, and Dependence: Learning; Wikler's Conditioning Theory of Drug Addiction.**

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RELAPSE. Although specific definitions of *relapse* vary across behaviors and diagnoses, the term in general refers to a return to a problematic behavior. Relapse is used to describe outcomes and stages in many fields, including substance use, sexual behaviors, eating disorders, mood disorders, and medical conditions. While each of these disciplines may assign some variation to the consideration of relapse, much consensus exists regarding its antecedents, process, and interventions.

Generally, after individuals have made a change regarding a problematic behavior (e.g., reduced or abstained from drinking alcohol, stopped pathological gambling, established a healthy diet), they are at risk for a return to the previous behavior. A brief, minor, or transient return is typically referred to as a lapse. Following this situation, one of two outcomes may follow. If individuals reestablish their goals and return to a positive change state, prolapse has occurred. If, by contrast, individuals reengage in the problematic activities, returning to pre-change behavior, they experience a relapse.

Due to varying definitions of *relapse* in research, relapse rates are difficult to generalize among substance abusers, let alone across fields. Some studies have indicated that relapse rates are relatively high among individuals seeking abstinence either with or without formal treatment. For example, studies have indicated that up to 60 percent of alcoholics, heroin addicts, and smokers relapse within three months of the end of treatment.

The cognitive-behavioral model of relapse originally proposed a linear series of antecedents and outcomes (if/then relationships) based on high-risk situations and individual predispositions. Subsequently, this theory evolved to incorporate a dynamic relationship between tonic processes, or chronic vulnerabilities, and phasic responses, or transient states. The interactions between these vulnerabilities and states either increases or decreases the risk of relapse for individuals in any given situation. For example, poor coping skills may interact with a temporary increase in negative affect and positive expectancies, resulting in a relapse. Conversely, significant social support may mediate risks related to dependence and family history, thus avoiding a relapse. This model considers the interaction of diverse influences such as physical withdrawal, cognitive processes, affective states, coping behaviors, family history, social support, and expectancies.

The dynamic model of relapse incorporates many previously disparate theories on the determinants of relapse. For example, high-risk situations are not limited to external events or circumstances (e.g., passing by a location where drugs are bought or used), but also incorporate enduring personal characteristics (e.g., low self-efficacy). A family history of substance abuse may increase risk of relapse, but its effects can only be fully understood under the broader context of high-risk situations. Furthermore, the consideration of affective states incorporates psychopathology and mood disorders, such as relationships between depression and relapse. Reactions to major life events are included through phasic affective states (e.g., grief) and cognitive processes (e.g., repetitive thoughts). Even classic learning theories and conditioning models are incorporated through the inclusion of withdrawal symptoms or cues paired with expectancies associated with engaging in the previous behavior (e.g., "I will feel less anxious/angry/sad if I drink").

Following exposure to a high-risk situation, individuals may successfully avoid or limit the problematic behavior, leading to an increase in self-efficacy and a lower risk of future relapse.

Conversely, if a lapse occurs, individuals are likely to experience either prolapse or relapse. Prolapse is associated with external, specific, and transient attributions of the lapse. For example, drinking after a stressful day at work will be attributed to the specific stresses experienced that day and a poor decision to drive by the local tavern. In this case, individuals are likely to learn from the mistake and take steps to increase future success. Conversely, relapse is associated with internal, global, and stable attributions referred to as the abstinence violation effect (AVE). In this case, the stressful day at work is seen as evidence that change is not possible due to inability to deal with any stress. The lapse is viewed as a personal failure, self-efficacy is diminished, and motivation to change is confounded by hopelessness (e.g., the conclusion that the lapse proved that the individual has no will power.)

Relapse prevention (RP) is a widely accepted and used treatment in each of the fields previously listed. Although RP looks different on the surface between treatment for cocaine dependence and treatment for depression, for example, the underlying theory remains consistent. RP seeks to identify potential high-risk situations as well as successful coping strategies. Given the infinite number of interactions for any individual, generalization is required to both identify high-risk situations and to avoid relapse. RP has substantial support in the literature both in its traditional cognitive-behavioral model as well as more recent combinations, including acceptance and mindfulness-based relapse prevention. Meanwhile, researchers continue as of 2008 to identify what works best for whom in which situations.

See also **Abstinence Violation Effect (AVE); Treatment, Behavioral Approaches to: Cognitive-Behavioral Therapy.**

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RELIGION AND DRUG USE. Drug use and religion have been intertwined throughout history, but the nature of this relationship has varied over time and from place to place. Alcohol and other drugs have played important roles in the religious rituals of numerous groups. For example, among a number of native South American groups, tobacco was considered sacred and was used in religious ritual, including the consultation of spirits and the initiation of religious leaders. Similarly, wine, representing the blood of Christ, has been central in the Holy Communion observances of both Roman Catholic and some Protestant churches. Considered divine by the Aztecs of ancient Mexico, the peyote cactus (which contains a number of psychoactive substances, including the psychedelic drug mescaline) is used today in the religious services of the contemporary Native American Church (Goode, 1984).

Although tobacco, alcohol, peyote, and other drugs have been important in the religious observances and practices of numerous groups, many religious teachings have opposed either casual use or the abuse of psychoactive drugs—and some religious groups forbid any use of such drugs, for religious purposes or otherwise. Early in America's history, Protestant religious groups were especially prominent in the temperance movement. Many of the ministers preached against the evils of drunkenness, and such well-known Protestant leaders as John Wesley, called for the prohibition of all alcoholic beverages (Cahalan, 1987). The Latter-day Saints' (Mormons) leader Joseph Smith prohibited the use of all common drugs, including alcohol, tobacco, and caffeine (in cola drinks, coffee, or tea), as did other utopian groups founded during

the Second Great Awakening of the early 1800s. Religious groups and individuals were also active in America's early (1860s–1880s) antismoking movement (U.S. Department of Health and Human Services, 1992). In contemporary American society, certain religious commitments continue to be a strong predictor of either use of or abstinence from drugs, whether licit or illicit (Cochran et al., 1988; Gorsuch, 1988; Payne et al., 1991). For example, Islam forbids alcohol and opium use but coffee, tea, tobacco, khat, and various forms of marijuana are not prohibited because they came into the Islamic world after the prohibitions were laid down. Indulgence in any debilitating substance is, however, not considered proper or productive. Christianity, Judaism, and Buddhism may not prohibit specific drugs, but they and most other widespread mainstream religious traditions also caution against indulgence in most substances. In our society, many who have indulged have sought the help of Alcoholics Anonymous (AA) or Narcotics Anonymous (NA)—both self-help groups founded on strong spiritual underpinnings.

This discussion is limited to conditions in the United States, focusing on potentially dangerous, abusive, and/or illicit patterns of drug use. Since such drug use is widely disapproved by most religious teachings and leaders, it is not surprising to find that those with strong religious commitments are less likely to be drug users or abusers. Moreover, research findings clearly show that religious involvement has been a protective factor, helping some adolescents resist the drug epidemics of the 1970s and 1980s.

Because religion has been found to be a protective factor against drug use and dependence and because our society is concerned with drug use among young people, much of the research linking religion with drug use focuses on adolescents and young adults. This age range is particularly important for several reasons. First, it is the period during which most addiction to nicotine begins; the majority of people who make it through their teens as nonsmokers do not take up the habit during their twenties or later (Bachman et al., 1997). Second, adolescence and young adulthood is the period during which abusive alcohol consumption is most widespread. Third, recent epidemics in the use of illicit drugs have been most pronounced among teenagers and young adults. Fourth, during this portion of the life span, many changes, opportunities, and risks occur; thus the structures and guidelines provided by religious commitment may be especially important in helping young people resist the temptation to use and abuse drugs. Finally, evidence that religious conversion is most likely to occur during adolescence (Spilka, 1991) makes this period particularly appropriate for research on the link between religion and drug use.

THE RELATIONSHIP BETWEEN RELIGIOUS COMMITMENT AND DRUG USE

Research investigating the relationship between religious commitment and drug use consistently indicates that those young people who are seriously involved in religion are more likely to abstain from drug use than those who are not; moreover, among users, religious youth are less likely than nonreligious youth to use drugs heavily (Gorsuch, 1988; Lorch & Hughes, 1985; Payne et al., 1991).

Figure 1 shows how drug use was related to religious commitment among high school seniors in 1979, 1989, and 1999. Individuals with the highest religious commitment were defined as those who usually attend services once a week or more often and who describe religion as being very important in their lives; individuals with low commitment are those who never attend services and rate religion as not important. Figure 1 clearly indicates that those with low religious involvement were more likely than average to be frequent cigarette smokers, occasional heavy drinkers, and users of marijuana and cocaine; conversely, those highest in religious commitment were much less likely to engage in any of these behaviors. Other analyses have shown that similar relationships exist for other illicit drugs (Bachman et al., 1986) and for other age groups (Cochran et al., 1988; Gorsuch, 1988).

Trends in Drug Use and Religious Commitment. Figure 1 presents data from three points in time, separated by ten-year intervals. It is obvious in the illustration that between 1979 and 1989, the proportion of high school seniors using the illicit drugs marijuana and cocaine declined markedly; also during that decade, the proportion reporting instances of heavy drinking declined appreciably, as did the proportion of frequent smokers. Between

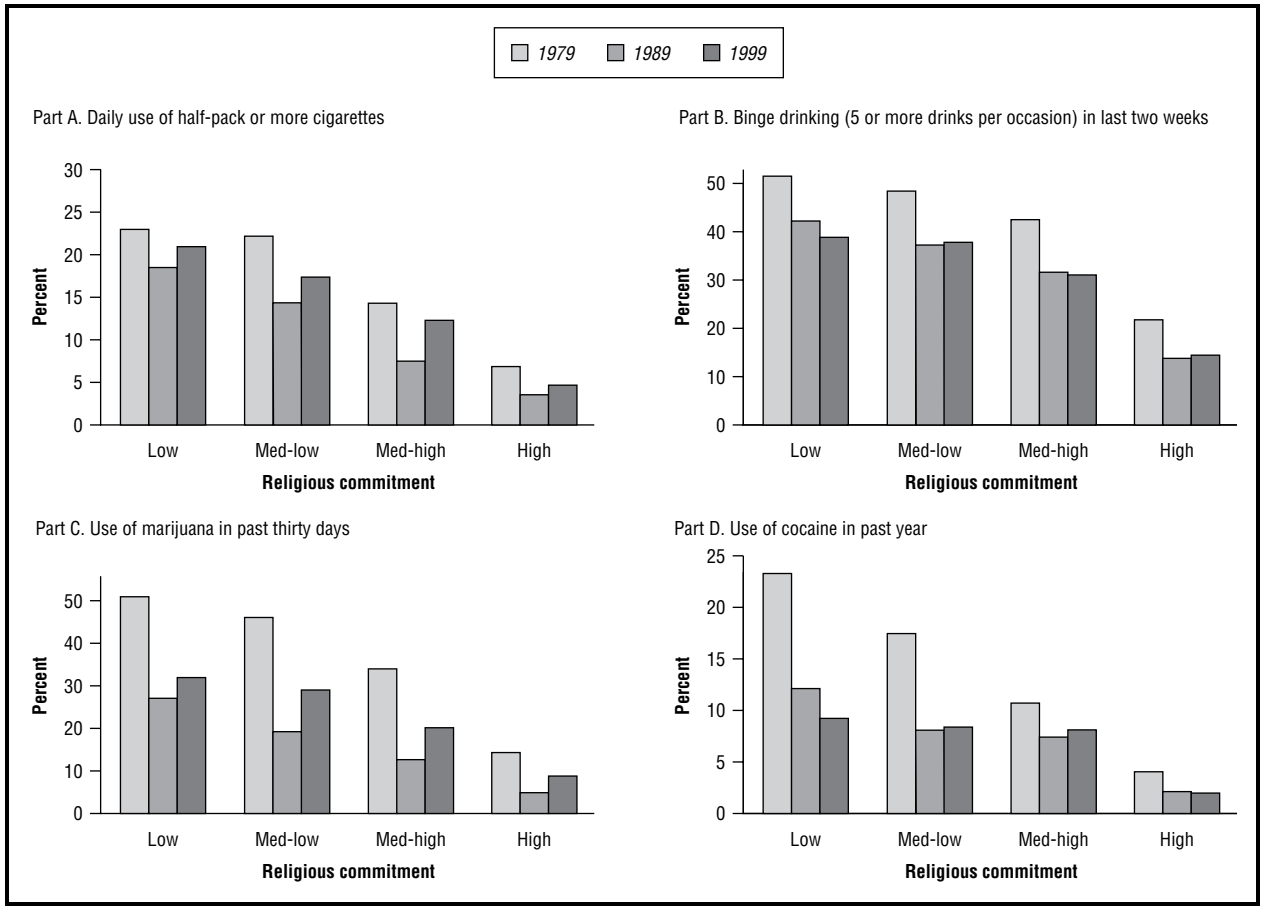

Figure 1. Drug use among high school seniors shown separately for four levels of religious commitment. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

1989 and 1999, the proportion of cigarette users and marijuana users rose somewhat; for year-to-year changes in substance use, see Johnston et al., (2000). For the present purposes, the most important finding in Figure 1 is that religion was linked to drug use at all three times, although the relationships appear a bit more dramatic during periods of heavier use.

Because high religious commitment is associated with low likelihood of drug use, it is reasonable to ask whether any of the decline in illicit drug use during the 1980s could be attributed to a heightened religious commitment among young people during that period. The answer is clearly negative, as illustrated in Figure 2. The same annual surveys that showed declines in drug use also indicated that religious commitment, rather than rising during the 1980s, was actually declining among high school seniors. It thus appears that other factors accounted for the declines in illicit drug use, factors such as the increasing levels of risk and the heightened disapproval associated with such behaviors (Bachman et al., 1988, 1990; Johnston, 1985; Johnston et al., 2000). Moreover, Figure 2 shows that religious commitment—especially ratings of importance—actually rose slightly during the 1990s, so it does not appear that the rise in use of some drugs during the 1990s is attributable to any further drop in religiosity.

Religion as a Protective Factor. The most plausible interpretation of the relationship between religion and drug use during recent years, in our view, is that religion (or the lack thereof) was not primarily responsible for either the increases or the subsequent decreases in illicit drug use. Rather, it appears that those with the strongest religious commitment were least susceptible to the various epidemics in drug use. Figure 3 (adapted from

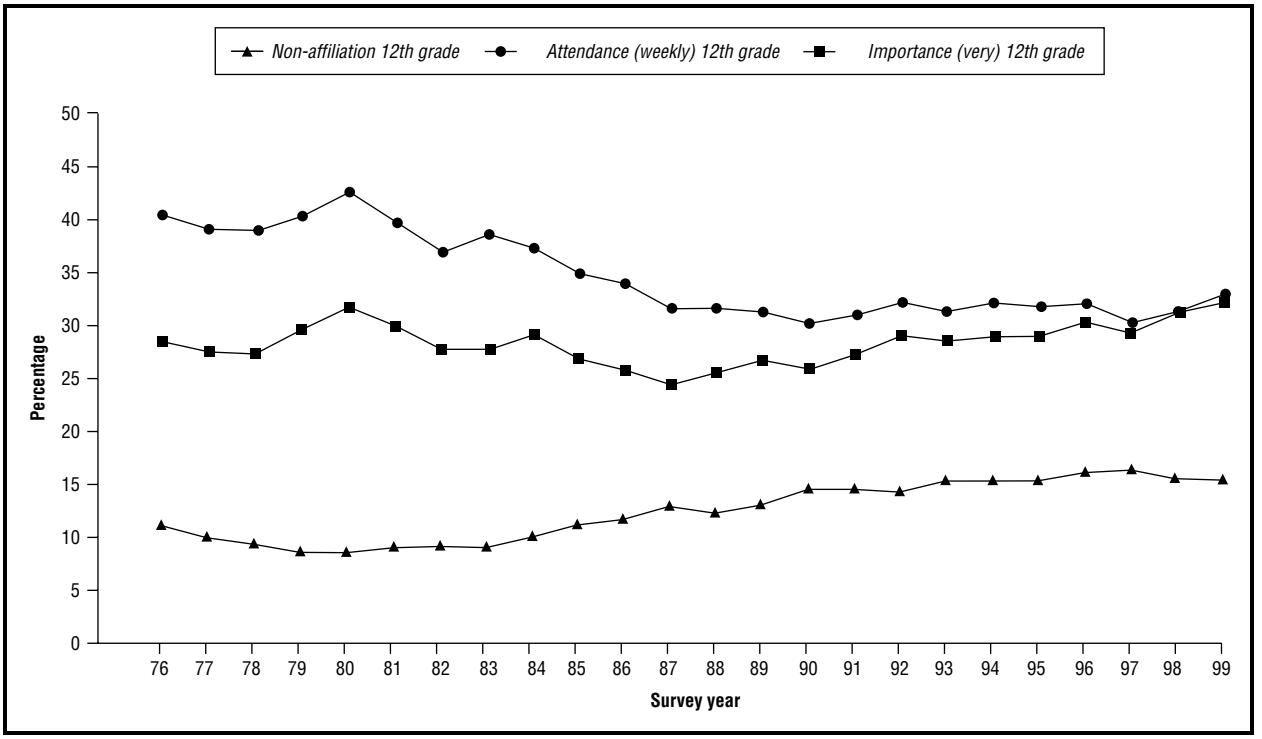

Figure 2. Trends in American youth religiosity. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Bachman et al., 1990) provides one example in support of that interpretation. The figure illustrates trends in cocaine use from 1976 through 1988, distinguishing among the four different degrees of religious commitment. Cocaine use roughly doubled between 1976 and 1979 among high school seniors and began to decline sharply after 1986. But the most important pattern in the figure for present purposes is that these historical trends in cocaine use were much more pronounced among those with little or no religious commitment. Put another way, it seems that strong religious commitment operated as a kind of protective factor, sheltering many youths from the waves of drug use sweeping the nation.

Denominational Differences. There are important differences among religious groups in the emphasis placed on drug use (Lorch & Hughes, 1988). In particular, the more fundamentalist Protestant denominations, as well as Latter-day Saints (Mormons) and African American Muslims, rule out the use of alcohol and tobacco and disdain illicit drug use. Research examining differences in drug use among young people finds that those who belong to fundamentalist denominations are more likely to abstain from drug use than are youth who belong to more liberal denominations (Lorch & Hughes, 1985). Analyses of the data on high school seniors (Wallace & Forman, 1998) corroborate the findings of earlier research; the number of young people strongly committed to fundamentalist denominations (e.g., Baptists) who use drugs is much lower than average and lower than the percentages for those strongly committed to other religious traditions.

Changes During Young Adulthood. Panel surveys that followed high school seniors up to fourteen years after graduation revealed that substance use often increases in response to such new freedoms as leaving high school and moving out of parents' homes, whereas use often decreases in response to such new responsibilities as marriage, pregnancy, and parenthood (Bachman et al., 1997). Additional analyses of these data reveal that religion continues to be strongly related to various forms of drug use during the late teens, twenties, and early thirties. These analyses reveal that religious attendance and importance change rather little for most individuals; but when changes in religiosity occur, there tend to be corresponding

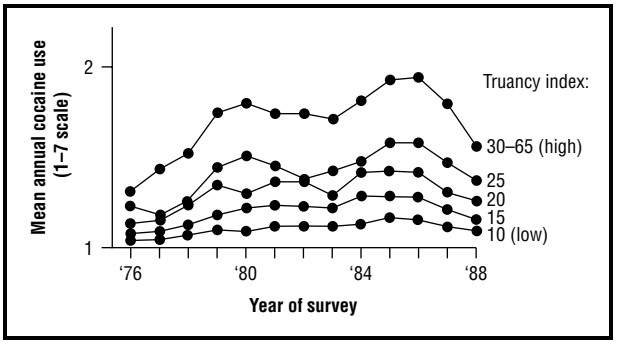

Figure 3. Trends in annual cocaine use shown separately for five levels of truancy among high school seniors. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

changes in substance use. Specifically, increases in religious commitment are correlated with declines in the use of alcohol and illicit drugs. Smoking behavior, on the other hand, is linked with religiosity during high school and thus also during young adulthood. However, after high school, smoking behavior is relatively little affected by changes in religiosity—presumably because by the time of young adulthood, most individuals who continue to smoke have become dependent on nicotine and find it very difficult to quit.

POSSIBLE CAUSAL PROCESSES

Since religious commitment is negatively related to drug use, it becomes important to understand the possible causal processes underlying that relationship. Wallace and Williams' socialization influence model (1997) specifies a number of possible mechanisms through which religious commitment might operate to influence adolescent drug use. The model postulates that health-compromising behaviors like drug use are the result of a dynamic socialization process that begins in childhood and extends throughout the course of life. According to the model, the family is the primary and first socialization influence, and a continuing source of socialization into the norms and values of the larger society. The model hypothesizes that religion, peer networks, and other contexts in which young people find themselves (e.g., schools) operate as key secondary socialization influences that impact drug use primarily indirectly through their influence on key socialization mechanisms, including social control, social support, values, and individual and group identity. Below, we describe some of the ways in which religion, parents, peers, and other potential causes might overlap to influence adolescent drug use. The socialization influence model further suggests that key aspects of adolescent religiosity, particularly denominational affiliation and religious attendance, are often under the control of parents and reflect the types of doctrinal beliefs, teachings, and adult and peer models to which parents want their children exposed.

Content of Religious Teaching. One possible causal process seems obvious: Most religious traditions teach followers to avoid the abuse of drugs. Restrictions vary, of course, from one tradition to another; and the greater emphasis on prohibition in fundamentalist denominations seems the most likely explanation for the lower levels of use among adherents. But even in traditions that do not explicitly or completely ban drug use, there is still much teaching ranging from respect for one's own body to family responsibilities to broader social responsibilities, all arguing against the abuse of drugs. Because all drugs, including cigarettes and alcohol, are illicit for minors, young people who are strongly committed to religion may abstain from drug use simply in obedience to the laws of the nation; but even more important, they are likely to act in obedience to what they perceive to be God's laws.

Parental Examples and Precepts. In addition to the direct teachings associated with attendance at religious services, young people raised in religious traditions are likely to be exposed to parents and other relatives who follow such teachings. Thus, part of the explanation for less drug use among religiously involved young people may be that their families reinforce the religious structures against use and abuse. A further factor may simply be availability; religious parents who do not drink, smoke, or use drugs will not have these substances in their homes, thus reducing the opportunity for young people to experiment with them.

Peer Group Factors. The dynamics operating within the family probably have their parallel in broader social contacts. That is, those who are strongly committed to religion probably associate with others holding similar views. Thus, the strongly religious are less likely to belong to peer groups that encourage experimentation with cigarettes, alcohol, and other drugs and more likely to participate in

Measure	Response[1]	Percent of substance use in the past month			
		Illicit drugs[2]	Marijuana	Cigarettes	Binge alcohol[3]
Religious beliefs very important part of life	Yes	7.6	4.8	7.9	8.1
	No	17.1	13.0	18.7	17.8
Religious beliefs influence decision making in life	Yes	6.9	4.2	7.0	7.2
	No	15.7	11.9	17.8	17.1
Important to share religious beliefs with friends	Yes	6.3	3.3	6.1	6.2
	No	11.6	8.4	12.8	12.6

[1]Illicit drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically.
[2]Illicit drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically.
[3]Binge alcohol use is defined as drinking five or more drinks on the same occasion (i.e., at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days.

Table 1. Past month use of selected substances by measure of religious beliefs among persons aged 12 to 17, by percentage, 2006. (Source: National Survey on Drug Use and Health, 2006, Office of Applied Studies, Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING.

peer networks and activities that do not involve drugs. Given the strong relationship between drug use by peers and an adolescent's own drug use, the norms of the peer group are especially important as predictors of whether a particular teenager will start using drugs (Jessor & Jessor, 1977).

Overlaps with Other Causes. Religious commitment among young people is correlated with a number of other factors known to relate to drug use. In particular, students who achieve good grades, who plan to go to college, and who are not truant are also less likely to use drugs as well as more likely to display high levels of religious commitment. These various factors are closely interrelated in a common syndrome (Dryfoos, 1990; Jessor & Jessor, 1977), and thus it is difficult to disentangle causal processes. Indeed, it could be argued that religious commitment is probably one of the root causes contributing to both educational success and the avoidance of drug use. Analyses of possible multiple causes of drug use (or abstention) have shown that religious commitment overlaps with other predictors, but only partially. In other words, although religious commitment may be part of a larger syndrome, it also appears to have some unique (i.e., nonoverlapping) impact on drug use.

RELIGION AND DRUG USE: CONCLUSION

The relationship between religion and drug use among young people is not completely straightforward. On the one hand, a considerable amount of research indicates that young people who are strongly committed to religion are less likely than their uncommitted counterparts to use drugs. On the other hand, data presented here and elsewhere suggest that religion has had relatively little impact on recent national declines in drug use among young people. Further examination of this relationship reveals that America's drug epidemic occurred primarily among those not affected by religion; highly religious youth were relatively immune to the plague that infected a significant portion of the nation's youth. Accordingly, we conclude that religious commitment has been, and continues to be, an effective deterrent to the use and abuse of licit and illicit drugs.

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See also **African Americans, Ethnic and Cultural Factors Relevant to Treatment for; Jews and Alcohol; Prevention.**

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JERALD G. BACHMAN
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REMOVE INTOXICATED DRIVERS (RID-USA, INC.). The organization Remove Intoxicated Drivers (RID-USA, Inc.) was founded in 1978 by Doris Aiken. This volunteer grassroots organization is devoted to deterring impaired driving, providing a variety of supports to victims and their families, monitoring court proceedings involving impaired or intoxicated drivers, influencing the development of nationwide legislation regarding alcohol use, and educating the public on the scope of impaired-driving and binge-drinking tragedies.

In November 1977, a young drunk driver in upstate New York killed Karen and Timothy Morris, who were 17 and 19 years old, respectively. When a local TV talk show host named Doris Aiken learned that the district attorney did not plan to prosecute the crime, she decided to form an organization to represent people affected by alcohol-related crimes. She learned that plea-bargaining in alcohol-related automobile accidents generally enabled impaired

drivers to remain on the road for more than three years before reaching the conviction and sentencing stages. In the late 1970s, an average of 25,000 people died annually in alcohol-related motor vehicle accidents, and the surviving drivers were, more often than not, allowed to retain their licenses and continue to operate motor vehicles. Aiken was able to obtain a start-up grant from the National Highway Traffic Safety Administration (NHTSA), and by 1982 her organization, RID-USA, had 75 chapters across 22 states.

RID-USA's victim-support activities, which are free, include providing long-term emotional support to victims of drunk-driving crashes (and to victims' families), counseling victims and accompanying them throughout all phases of the criminal prosecution of the offender, assisting victims in obtaining compensation, and referring victims and their families to appropriate supportive agencies. Court monitoring and research activities include monitoring the efforts of police, prosecutors, magistrates, and judges in drunk-driving cases through research and analysis of local court records, and then reporting these findings to the public.

RID-USA's public awareness and education activities are extensive. Members organize public meetings; present educational talks to community and religious organizations; participate in forums, exhibits, and media events; supplement high school driver-education classes; and support Students Against Destructive Decisions (SADD; originally named Students Against Driving Drunk) and other similar student groups. They also study and report on alcohol-related vehicle and traffic laws, support concepts such as designated-driver and alcohol-server education, and promote the Sane National Alcohol Policy (SNAP) campaign, which advocates raising taxes on alcohol, curbing campus beer promotions, and airing public-service advertising to counter broadcast alcohol commercials. Among its media campaigns, RID-USA has developed and implemented a multimedia public awareness and education program about binge drinking and alcohol poisoning, particularly among underage drinkers. RID-USA, which celebrated its 30th anniversary in 2008, is organized into autonomous chapters, with more than 150 chapters in 41 U.S. states and a national group in France.

See also **Accidents and Injuries from Alcohol; Alcohol; Crime and Alcohol; Dramshop Liability Laws; Driving, Alcohol, and Drugs; Driving Under the Influence (DUI); Mothers Against Drunk Driving (MADD).**

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RESEARCH

This entry includes the following essays:

AIMS, DESCRIPTION, AND GOALS

There has always been interest in information related to drugs and alcohol and their effects. Reports on the use of psychoactive substances first appear in ancient manuscripts. The properties of marijuana were first described in 2732 BCE in a Chinese book on pharmacy. A description of the effects of opium has been found in an Egyptian papyrus scroll dating from about 1550 BCE. In almost every culture, the uses of alcohol are documented in both oral and written traditions, often going back to antiquity—the Bible, for example, mentions both the use and abuse of wine. Although people have made observations on these substances for thousands of years, much of that information is regarded as *anecdotal*, that is, based on the observation of specific incidents rather than from any systematic evaluation of the facts. The problem with anecdotal observation is that it

cannot always be generalized, that is, it cannot be used reliably to predict future events or behavior.

Scientific research, by contrast, employs the techniques of the *scientific method* to generate knowledge. When researchers use the scientific method, they may begin with an anecdotal observation to formulate their initial hypothesis, but from there the process changes. Instead of generalizing from the anecdotal evidence, the scientific researcher designs an experiment to test the prediction generated from the observation, performs the experiment, collects and analyzes the data, and only then arrives at a conclusion. The goal of current research into substance abuse, then, is to apply the techniques of the scientific method to solving the problems related to the use of both alcohol and drugs of abuse. Of course, there are limits to the use of the scientific method when studying human beings. For example, scientists cannot ethically conduct experiments in which some women are exposed to cocaine while pregnant and others are not. They must instead use animal models for these experiments, which can only approximate, rather than reproduce exactly, what occurs in humans. Other experiments are not economically or practically feasible. For example, a researcher may want to follow research subjects (people who have agreed to participate in a research experiment) over a period of five years to learn about the long-term effects of a medication. Unfortunately, each additional visit a subject makes to the clinic adds to the expense of the project and in the meantime the subjects themselves may no longer be available to complete the visits. The constraints of the situation may result in only a brief period of follow-up and thus limit the conclusions that may be drawn from the data.

Substance abuse research is no different from any other sort of scientific endeavor: The process is not always orderly. Critical observations by clinicians frequently provide basic researchers with important insights, which guide the research into new channels. Observations in one science often lead to breakthroughs in other areas. It is important to understand that the benefits of research may not be immediately obvious. Some research that seems promising may lead to a disappointing dead-end, whereas other lines of research may yield surprising results. Often, the research process is much like that of assembling a jigsaw puzzle: Many scientists contribute pieces to the puzzle, creating snapshots of parts of the problem, until one individual assembles them into a coherent picture that answers a larger question. The physicist Sir Isaac Newton modestly noted that his own theories came from standing on the "shoulders of giants," that is, he built on the work of scientists who preceded him. No less is true of early-twenty-first-century substance abuse research.

WHAT WE NEED TO KNOW

Most substance abuse research is a consequence of public health and social concerns. With millions of people using and abusing many different substances, and because of the close association between acquired immune deficiency syndrome (AIDS) and drug abuse, as well as between drug use and crime, it is imperative to know just how dangerous—or not dangerous—any given drug is to public health and safety. For economic as well as medical reasons, it is essential to find the most effective ways to use health-care resources to prevent and treat substance abuse. So many questions still exist that no one scientific discipline can answer them all. The answers must be found through studies in basic chemistry, molecular biology, genetics, pharmacology, neuroscience, biomedicine, physiology, behavioral science, epidemiology, psychology, economics, social policy, and even international relations. From a social standpoint, the first question for research must be: How extensive is the problem?

Surveys and other indicators of drug and alcohol use are the tools used by epidemiologists to determine the extent and nature of the problem, or to find out how many people are abusing exactly which drugs, how often, and where. As the dimensions of the problem are defined, basic scientists begin their work, trying to discover the causes and effects of substance abuse at every level, from the movement of molecules to the behavior of entire human populations. Chemists determine the physical structure of abused substances, and then molecular biologists study how they interact with the subcellular structures of the human body. Geneticists try to determine which components, if any, of substance abuse are inherited. Pharmacologists determine how the body handles abused substances and, in turn, the effects of those substances on the body. Neuroscientists examine the effects of

drugs and alcohol on the cells and larger anatomical structures of the brain and other parts of the nervous system. As these structures control human thoughts, emotions, learning, and perception, psychologists and behavioral pharmacologists study the drugs' effects on these functions. Cardiologists and liver and pulmonary specialists study the responses of heart, liver, and lungs, respectively, to drugs and alcohol. Immunologists examine the consequences of substance abuse for the immune system, a study made critical by the AIDS epidemic. The conclusions reached through these basic scientific inquiries guide clinicians in developing effective treatment programs.

In considering drug abuse, people have long wondered why so many plants contain substances that have such profound effects on the human brain and mind. Surely, people were not equipped by nature with special places on their nerve cells (called receptors) for substances of abuse—on the off chance that they would eventually smoke marijuana or take cocaine or heroin. The discovery in the late 1960s that animals would work to obtain injections or drinks of the same drugs that people abuse was an important scientific observation; it contributed to the hypothesis that there must be a biological basis for substance abuse.

These observations and this reasoning led scientists to look for substances produced by people's own bodies (endogenous substances) that behave chemically and physiologically like those that people put into themselves from the outside (exogenous substances), such as alcohol, nicotine, marijuana, cocaine, and other drugs of abuse. When receptors for endogenous substances were discovered—first for the opiates and then later for PCP, cocaine, marijuana, and LSD—their existence helped establish the biological basis for drug abuse. So did the evidence supporting a genetic component for certain types of alcoholism. These discoveries by no means negate the extensive behavioral and social components of substance abuse, but they do suggest a new weapon in dealing with the problem—that is, the possibility of using medication, or a biological therapy, as an adjunct to psychosocial therapies. Asserting a biological basis for substance abuse also removes some of the social stigma attached to drug and alcohol addiction. Since drug dependence is a disorder with strong biological components, society begins to understand that it is not merely the result of weak moral fiber. Armed with information that was derived initially from basic research, clinical researchers in hospitals and clinics can test and compare treatment modalities, looking for the best balance of pharmacological and psychosocial methods to rehabilitate individuals suffering from addiction. Finding the right approach for each type of patient is an important goal of treatment research, because patients frequently have a number of physical and mental problems besides substance abuse. The development of new medications to assist in the treatment process is an exciting and complex new frontier in substance abuse research.

The best way to prevent the health and social problems associated with substance abuse has always been an important research question. Insights gained from psychological and social research enable us to design effective prevention programs targeted toward specific populations that are particularly vulnerable to substance abuse for both biomedical and social reasons. Knowing the consequences of substance abuse often helps researchers to formulate prevention messages. For example, the identification of fetal alcohol syndrome (FAS), a pattern of birth defects among children of mothers who drank alcohol heavily during pregnancy, was a major research contribution to the prevention message aimed specifically at pregnant women.

Drug abuse prevention research has assumed a new urgency with the realization, brought about by epidemiologists and others, that the human immunodeficiency virus (HIV) is blood-borne—spread by sexual contact and by drug abusers who share contaminated syringes and needles. HIV-positive drug users then spread the disease through unprotected sexual intercourse. Public education about drug abuse and AIDS must use the most powerful and carefully targeted means to reach the populations at greatest risk for either disease, and these means can be determined only by the most careful social research and evaluation methods.

METHODS

The range of methods employed by scientists studying substance abuse is as wide as the range of methods in all of the biological and social sciences. One important method is the use of animal models of

behavior to answer many of the questions raised by drug and alcohol use. Animal models are used in virtually every field of biomedical research, but the discovery that animals will, for the most part, self-administer alcohol and drugs of abuse meant that there was great potential for behavioral research uncontaminated by many of the difficult-to-control social components of human research. The results of animal studies have been verified repeatedly in human research and in clinical observation, thus validating an animal model of human drug-seeking behavior.

Another important method is controlled clinical trials, in which one treatment method is compared to another. In controlled clinical trials, research subjects are randomly assigned to one of two or more treatment situations, allowing comparisons to be drawn that are not confounded by other factors. For example, patients can be assigned randomly to treatment with a medication, counseling, both medication and counseling, or neither medication nor counseling. Comparison of the groups' response to treatment can determine the efficacy of the medication both alone and in the context of counseling.

Drug and alcohol abuse research is conducted by individuals with many different qualifications, but mostly by physicians and people with doctoral degrees in a variety of disciplines. They work with animals and with patients in university and federally funded laboratories, as well as in privately funded research facilities, in offices, and in clinical treatment centers. Other sites include hospitals, clinics, and sometimes schools, the streets, and even advertising agencies when prevention research is being conducted.

FUNDING

Who pays for substance abuse research has always been an important issue. Most of the drug and alcohol abuse research in the world is supported by the U.S. government. One of the federally funded National Institutes of Health—the National Institute on Drug Abuse (NIDA)—funds the majority of drug abuse research conducted in the United States and abroad. In 2007 this amounted to nearly $1 billion, which supported NIDA's own intramural research at the Addiction Research Center and the research done in universities under grants awarded by the institute. NIDA's sister institute, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), plays a parallel role in funding alcohol abuse research. In 2007 it funded $436 million of alcohol research.

Many other U.S. government agencies also have important roles in sponsoring and conducting substance abuse research. For the most part, state and local governments do not sponsor substance abuse research, although they distribute much of the funds for treatment and prevention programs. Other countries, most notably Canada, sponsor basic clinical and epidemiological substance abuse research within their own universities and laboratories, but none does so on a scale that is comparable to that of the United States. Private foundations and research institutions such as the Salk Institute for Biological Studies, Rockefeller University, and the Scripps Clinic and Research Foundation use their own funds, as well as federal grant support, to pay for their research endeavors. Pharmaceutical companies also support some substance abuse research—mostly clinical work related to medications being developed for use in the treatment of drug and alcohol abuse. The U.S. government also sponsors much of the work of medications development for substance abuse.

See also **National Survey on Drug Use and Health (NSDUH); Research, Animal Model: An Overview; Substance Abuse and AIDS; U.S. Government; U.S. Government Agencies.**

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CLINICAL RESEARCH

Clinical research consists of multiple approaches seeking to describe, understand, predict, and/or change human health and behavior. Although the focus here is limited to research with humans, experiments with animals frequently lay the foundation for human studies. Furthermore, although clinical research methods are widely used in all branches of medical science, we will review the primary types of clinical research relevant to alcohol and drug abuse: social and behavioral research, brain studies, genetic and epidemiological studies, psychotherapeutic interventions, clinical drug trials, and combinations of these strategies. While many studies employ a large sample size and traditional quantitative methodology, case studies and phenomenological/qualitative research procedures also expand our knowledge and contribute to the scientific literature. We will begin with a discussion of ethics in clinical research and conclude with the dissemination and practical applications of findings.

Ethical issues are paramount in human research. Such issues are important whether a study involves participants answering personal questions anonymously or undergoing invasive experimental surgery. Most research is subject to review by an Institutional Review Board (IRB) prior to implementation to ensure the protection of its participants. Even exempt studies are typically required to obtain their exemption through an IRB. Although the specific IRB changes based on the funding mechanism and where the research will take place, some general guidelines apply across reviews. The Belmont Report (*Ethical Principles and Guidelines for the Protection of Human Subjects of Research*), created in 1979, embodies the three main principles that guide protections for human subjects in the United States: respect for persons, beneficence, and justice. Respect for persons requires that participants' autonomy be protected, that they are treated with respect, and that they provide informed consent for participation. The IRB ensures that volunteers understand their rights, the research's potential risks and benefits, and understand what to do should they need assistance or additional information. Although consent applies to legally competent adults, assent (or permission) is typically sought from participants under 18 years of age or those deemed legally incompetent to make medical decisions. Beneficence requires that the benefits of the research are maximized, while the risks to the research subjects are minimized. Often, laboratory results or pilot studies are required to demonstrate potential benefits and risks as well as to support the scientific merit of the proposal. Justice requires that the costs and benefits of the research be distributed equally throughout the population. Finally, the IRB monitors the study in an ongoing way, requiring approval for modifications, while ensuring the continued safety of participants.

Some types of research seek to simply observe and record behavior. Many social and behavioral studies use an observational approach to define, identify, and log types of behavior. These studies provide a foundation for further studies by illustrating problematic (or beneficial) behaviors, providing frequency estimates, and developing a baseline of natural occurrences. These studies can vary from naturalistic observation to nationally representative questionnaires. In addition to recording behavior, investigators often manipulate a variable to explore alternate behaviors. These studies test hypotheses related to understanding and predicting behaviors. For example, a social experiment might explore individual reactions to criticism while in a relaxed versus a stressed state. Understanding how external stimuli relate to behavior can ultimately provide opportunities to change behavior.

Brain imaging research is another area of investigation that seeks to describe or identify factors related to behavior. Advances in neuroimaging have allowed investigators to isolate the brain structures involved in specific activities. Functional magnetic resonance imaging (fMRI), for example, has greatly increased knowledge of brain regions that are activated in relation to specific mood states, behaviors, etc. Areas of the brain that could have only been viewed in animals or on postmortem examinations are now detectable in healthy functioning individuals. These studies combine biology and psychology, and can provide empirical evidence of changes within or between individuals.

Genetic and epidemiological studies extend description and seek causes or correlates of disease. Epidemiological studies, in general, focus on a specific disorder and attempt to identify risk factors. For example, alcohol use disorders are associated with many exposures and behaviors in adolescence, even if the disorder does not present until decades later. Genetic studies are a specific type of epidemiology, looking at the role of biological markers in risk for disease. There continues to be much debate about the role of genetics in many disorders, even with increases in technology and the ability of investigators to examine genetic influences. The Human Genome Project and subsequent large-scale efforts to understand the role of genetics in human health and disease have resulted in a veritable explosion of new knowledge in this area.

INTERVENTIONAL STUDIES

Studies that seek to manipulate the occurrence or trajectory of a disorder fall into the category of clinical trials. Other types of clinical trials can include prevention, diagnostic, screening, and quality of life trials, although the focus here is limited to treatment trials. Two primary types of clinical trials are considered: behavioral (psychotherapeutic) and medical (drug) interventions. While many of the same goals and requirements apply to each, the nature of the study designs can vary. Both types of studies are bound by the same ethical guidelines and requirement for IRB approval. Study designs also tend to be similar in these trials, with emphasis placed on randomized studies with adequate sample size to allow for valid conclusions. One clear difference between study designs is the ease with which a blinded study can be conducted. In a double-blind study, common in drug trials, neither the participant nor the investigator is aware of whether the substance administered is the active drug or a placebo. In psychotherapy research, it is virtually impossible for a provider to not know which treatment is being provided. Rather than using a blinded design, psychotherapy research typically includes a comparison group to account for natural progression or improvement. In either case, ethics require that participants be made aware of the potential to be assigned to either group as well as any risks they might endure if assigned to each of the specific groups.

Psychotherapy research attempts to identify, standardize, and test psychotherapeutic interventions for efficacy and effectiveness. These studies focus on changing or modifying behavior. Efficacy refers to the internal validity of an intervention; it scientifically evaluates a specific treatment for a specific population. These studies, referred to as randomized controlled trials (RCT), lead to the identification of empirically supported treatments (EST) or empirically validated treatments (EVT). These studies will randomly assign an adequate number of screened participants with a specific disorder to receive either the intervention that is being tested, an alternate intervention, and/or a no-treatment or wait-list control group. For example, participants meeting criteria for drug dependence might be randomized to receive a brief cognitive-behavioral (CBT) intervention, a twelve-step program, or an attention-control (i.e., one in which the participant receives comparable attention, but not the specific intervention being evaluated). The interventions in these studies are typically standardized and therapist adherence is monitored. Outcomes of these studies frequently inform healthcare practices and insurance coverage for services. These closely monitored and rigorous studies are more likely to receive and maintain funding as well as have their findings published in prestigious journals. Although the benefits of efficacy studies are great, the role of effectiveness studies is equally important. At this stage, studies are typically transferred from a controlled setting to the "real world." With the addition of covariates such as comorbid conditions, the specificity and ability to detect change based on the intervention are typically lessened, while issues of practical application and generalizability are increased. The dissemination of research and applicability to practice will be discussed below.

Clinical trials testing drugs or other medical interventions also seek to identify ways to change or manipulate behaviors or conditions. Drug trials progress through four individual phases, which occur after animal testing shows the drug to be safe enough for human administration. Phase I studies assess the safety of a drug by testing it in a small number of healthy individuals and provide a range of doses that are well tolerated in humans. Phase II is concerned with initial efficacy in affected individuals and may take months to years to complete. This phase of the study involves randomized and blinded conditions with several hundred participants. If a drug has been determined to be safe and potentially efficacious, it

progresses to Phase III and is tested in several hundred to several thousand participants. Studies in this phase, which can last several years, are also typically randomized and blinded, and inform a decision by the Food and Drug Administration (FDA) in the United States or similar regulatory agencies in other countries concerning the suitability of the drug for use in the general population. Phase IV studies are employed to test a drug against other drugs on the market, to monitor long-term effects, and/or to establish cost-effectiveness. Specific examples of Phase IV studies are the clinical trials of naltrexone for the treatment of alcohol dependence, after the medication had been approved for the treatment of opiate dependence.

In the early twenty-first century many studies combine different types of research, and funding agencies increasingly encourage collaboration. For example, the COMBINE study included medications, behavioral interventions, and combinations of each to identify the effectiveness of each treatment independently and together. Large studies such as this, with adequate sample sizes, can also incorporate epidemiological and demographic factors to determine what works best and which intervention or combination is efficacious for which participants.

DISSEMINATION AND PRACTICAL APPLICATIONS

Of the myriad clinical research studies ongoing at any given time, the results from only a small proportion of them ever reach clinical practitioners, and a smaller number are distributed to the general public. Given the importance placed on rigorous design, some studies are deemed unsuitable for publication in peer-reviewed journals. In addition, regardless of the design, the results of studies that do not find significant outcomes are often not published. These situations can lead to an exaggerated opinion of the effectiveness of treatment methods. There are also concerns that a conflict of interest or bias could influence the distribution of specific findings. For example, pharmaceutical companies typically fund their own studies, and they have a financial interest in having favorable outcomes disseminated. Although much behavioral research is financed by government agencies and other sources, an investigator may be biased by a conflict of interest related to ongoing support from public or private sources. Double-blind studies and control groups can reduce an investigator's influence on outcomes, and peer-review or government analysis can regulate the consistency and rigor of design. Nonetheless, conflicts of interest in clinical research, particularly treatment studies, have begun to take center stage in academic and regulatory affairs.

Even when a study passes all of the required levels of review, is completed, and its findings are accepted for publication in a peer-review journal, many barriers to implementation exist. Clinical research should not only further the science underlying the diagnosis and treatment of addictive disorders, but must also be designed to inform practice. Effectiveness trials of behavioral interventions and Phase IV drug trials are crucial to transferring research into practice.

IN SUMMARY

Clinical research employs a variety of methods, from observation to intervention. The role of clinical research is to inform practice by improving our understanding of the mechanisms of disease and its diagnosis, and efficacious treatment. There are many ethical considerations in the conduct of clinical research, and IRB review provides a system of checks and balances to ensure informed consent by participants and their ongoing protection throughout the research process. Advances in technology will continue to improve our capacity to identify biological and genetic factors that underlie addictive behavior and disorders, and epidemiological studies, including clinical trials, will continue to inform interventions to improve the health and welfare of addicted individuals.

See also **Abuse Liability of Drugs: Testing in Humans; Abuse Liability of Therapeutic Drugs: Testing in Animals; Brain Structures and Drugs; Clinical Trials Network; Diagnosis of Substance Use Disorders: Diagnostic Criteria; Epidemiology of Alcohol Use Disorders; Imaging Techniques: Visualizing the Living Brain.**

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DIANE E. LOGAN

DEVELOPING MEDICATIONS TO TREAT SUBSTANCE ABUSE AND DEPENDENCE

Dependence on drugs, alcohol, or tobacco is difficult to treat, and practitioners have tried many approaches in their attempts to arrive at successful treatments. One approach is to develop medications, or pharmacological treatments. This approach is most effective when the medication is given along with behavioral treatments. These behavioral treatments help the individual cope with the underlying etiology of his or her drug use and the problems associated with drug use; they may also help to ensure compliance in taking the medication that is prescribed.

PERPETUATION OF DRUG ABUSE: EUPHORIA AND WITHDRAWAL

Many people who are drug or alcohol dependent want to stop their habit, but typically they have a difficult time doing so. There are at least two reasons for this difficulty. First, the drugs produce pleasant or euphoric feelings that the user wants to experience again and again. Second, unpleasant effects can occur when the drug use is stopped. The latter effect, commonly known as withdrawal, has been shown after prolonged use of many drugs, including alcohol, opiates (such as heroin), sedative hypnotics, and anxiety-reducing drugs. Other drugs, such as cocaine and even caffeine (coffee and cola drinks), nicotine (cigarettes), and marijuana, are also believed to be associated with withdrawal effects after prolonged use. These unpleasant withdrawal effects are alleviated by further drug use. Thus drugs are used and abused because they produce immediate pleasant effects (positive reinforcement) and because the drug reduces the discomfort of withdrawal (negative reinforcement).

The symptoms of withdrawal are fairly specific for each drug and include physiological effects and psychological effects. For example, alcohol withdrawal can be associated with shaking or headaches, and opiate withdrawal with anxiety, sweating, and increases in blood pressure, among other effects. Withdrawal from cocaine may cause depression or sadness, withdrawal from caffeine is associated with headaches, and withdrawal from nicotine often produces irritability. All drug withdrawals are also associated with a strong craving to use more drugs. Much work has been done to document the withdrawal effects from alcohol, opiates, benzodiazepines, and tobacco; however, as of 2008 withdrawal from cocaine or other stimulant drugs has been less well documented.

NEURAL CHANGES WITH CHRONIC DRUG USE

Both withdrawal and the pleasant or euphoric effects from drug use occur, in part, as a result of the drug's action on the brain. The immediate or acute effects of most drugs of abuse involve areas of the brain that have been associated with reward or pleasure. These drugs stimulate areas normally aroused by natural pleasures such as eating or sexual activity. Long-term, or chronic, drug use alters these and other brain areas. Some brain areas will develop tolerance to the drug effects, so that greater and greater amounts are needed to achieve the original effects of the drug. Some examples of drug effects to which tolerance develops are the analgesic, or painkilling, effect of opiates and the euphoria or pleasure-producing effect of most drugs of abuse, which are probably related to their abuse potential.

Because some brain areas may also become sensitized, an original drug effect will either require a lesser amount of the drug to elicit the effect when the drug is used chronically or the effect becomes greater with chronic use. This phenomenon has been studied most extensively in cocaine and other stimulant use. Stimulants are associated with behavioral sensitization of motor activity in animals, and paranoia (extreme delusional fear) in humans. There are physiological

effects that develop tolerance or sensitization as well. For example, the chronic use of cocaine sensitizes some brain areas so that seizures are more easily induced, an effect that is called *kindling*. Other health risks of drug use are addressed below.

In addition to these more direct acute and chronic drug effects, another phenomenon occurs with long-term drug use. This phenomenon is the conditioned drug effect, in which the environmental or internal (mood states) cues commonly presented with drug use become conditioned or psychologically associated with drug use. For example, when angry, a drug addict may buy or use drugs in a certain place with certain people. After frequently taking drugs under similar conditions, the individual can experience a strong craving or even withdrawal when in the environment in which he or she has taken drugs or feels angry. When the individual tries to stop using drugs, exposure to these conditioned cues can often lead to relapse because the craving and withdrawal effects are so powerful. Very little research has been done as of 2008 on the neural bases of the conditioned withdrawal; thus, it is not known whether these conditioned effects are mediated by similar or different neural mechanisms than the primary pharmacological withdrawal from these drugs.

RESEARCH ON DRUG EFFECTS

Many of these acute and chronic effects of drugs on the brain have been investigated in animal research, which allows greater control over the research, including manipulations of drug exposure. A number of animal models are used to assess drug preferences, and, since most drugs that humans abuse are also preferred by animals, these models are useful for understanding human drug abuse. Moreover, animal research allows scientists to directly study the various areas of the brain that are involved in drug use. In addition, recent technological advancements in noninvasive imaging have allowed scientists to look at pictures of the brains of humans while they are being administered drugs or while they are withdrawing from drugs. This human work has provided information about the drug effects on the brain and validated the information gained from animal research.

Another useful line of research in assessing the effects of drugs involves human laboratory studies. In one type of study, research volunteers who have had experience with the abused drugs are given a specific drug (e.g., morphine), and various psychological and physiological measurements are obtained. The psychological measurements can include reports from the subject on the effects of the drug as well as more sophisticated behavioral measures that tell the experimenter how much the drug is preferred. Another type of human laboratory research entails the study of the effects of drug withdrawal. For opiates, withdrawal can be precipitated by an opiate antagonist drug (e.g., naltrexone), and withdrawal signs and symptoms are measured. For other drugs (such as cocaine), withdrawal is more difficult to measure because little is known about their withdrawal syndromes.

Some of what scientists have learned from such studies includes delineating specific brain areas as well as the neurotransmitters (the chemicals released by the brain cells) involved in drug use and withdrawal. Thus, when specific neurotransmitters are identified as playing an important role in drug use or withdrawal, scientists can administer experimental drugs that act on these neurotransmitters to see if the animals will alter their drug preference or show less severe withdrawal signs. Researchers can also give these experimental drugs to human research volunteers to see if the medication alters the subjects' perception of or behavior toward the abused drug, or if it alleviates withdrawal symptoms. If the results from these animal and human laboratory studies are promising, then these agents can be tested on treatment-seeking, drug-dependent individuals in clinical trials. This latter type of research is more time-consuming and expensive than the laboratory studies, but it helps provide an answer to the ultimate question: Does this medication help an individual stop abusing drugs?

APPROACHES TO DEVELOPING MEDICATIONS FOR DRUG ABUSE

Researchers can use the knowledge gained from animal and human studies of the effects of drugs on the brain as they develop medications for alcohol and drug dependence. Most likely, one medication will be needed to help detoxify the drug-dependent individual and a second medication to help sustain abstinence from drug use. This two-phase medication regimen is used for opiate and alcohol treatment, and it may ultimately be the approach used for countering dependency on other drugs, such as cocaine, sedatives, and nicotine. In theory, a pharmacological treatment agent or medication would block or reduce

either the acute, rewarding effect of the drug or the discomfort of withdrawal. In practice, few treatment drugs have been found to be very effective in sustaining abstinence from drugs or alcohol.

Any pharmacological agent should be able to be given orally, as this is much easier than other routes of administration, such as injections. The agent itself must be medically safe and not enhance any of the health risks associated with illicit drug use, since the individual may illicitly use drugs while being maintained on the treatment agent. Finally, the pharmacological treatment agent must be acceptable to the patient. That is, if the agent causes undesirable side effects, individuals tend not to take it.

Research in the early twenty-first century on the effects of alcohol and drugs on the brain and on treatment outcome holds great promise for the identification of effective pharmacological agents. This search process will necessarily include the animal and human laboratory studies mentioned as well as medicinal chemistry research. Medicinal chemistry research is used to develop new compounds that have similar but slightly altered chemical structures to the abused drugs or to the neurotransmitters that mediate the drug or alcohol effects. These new compounds are then tested in animals to see if they produce therapeutic effects. These effects include having a low potential for abuse and attenuating the effects of the abused drug under study, preferably in a way that would lead to decreased drug abuse.

EXAMPLES OF MEDICATIONS USED TO TREAT DRUG ABUSE

Several types of medications have been developed for countering various kinds of dependencies.

Opiate Dependence. Some of the best examples of pharmacotherapies for drug abuse were developed for opiate addicts. One of the first pharmacological agents used to treat opiate addicts is methadone. Methadone itself is an opiate drug and effectively reduces or blocks the withdrawal discomfort brought on by discontinuing use of heroin or other illegal opiates. Although methadone is itself addictive, it is delivered to the opiate-dependent patients in a facility with psychological and other medical and support treatments and services. Methadone is safer than opiates obtained illegally, in part because it is given orally.

Because illegal opiates are often injected by addicts, they can lead to many diseases, including AIDS and hepatitis, if the needles are shared with an infected person. Illegal drug use is expensive, and many addicts steal to support their habit. Moreover, since drugs obtained illegally vary in their quality and purity, there is a greater chance of getting an overdose that produces severe medical problems and, perhaps, death. Thus methadone decreases the need to use illegal opiates, as a result of its ability to relieve withdrawal as well as to block the effects of other opiates by cross-tolerance. Moreover, it reduces the health risks and social problems associated with illegal opiate use.

Another treatment drug that was developed for opiate dependence and abuse is naltrexone. This agent blocks the ability of the opiate drug to act on the brain. Thus, if a heroin addict maintained on naltrexone injects heroin, he or she will not feel the pleasant or other effects of the heroin. The principle behind this approach is based on research suggesting that drug use is continued, despite the dire consequences, because of the euphoria associated with its use. Once maintained on naltrexone, the addict may forget this association because the drug can no longer produce these effects. Unfortunately, although naltrexone works well for some, others simply discontinue using the naltrexone in order to get high from drugs again.

Before opiate abusers can be maintained on the medication naltrexone, they must be detoxified from the opiate drugs in their systems. Although abstaining (going cold turkey) from heroin use for several days accomplishes detoxification, the withdrawal process is difficult because of the physical distress it causes. Thus, another detoxification method was developed in which the withdrawal is precipitated, or triggered, with naltrexone, while the symptoms are treated with another medication, clonidine.

When withdrawal is precipitated, the symptoms are worse than that seen with natural withdrawal, but the symptom course is much briefer. Moreover, clonidine helps alleviate the symptoms, to make this shorter-term withdrawal process less severe. Finally, buprenorphine is a medication that is effective in reducing opiate use, and at higher

doses is able to block the *high* or pleasant effects of opiates like heroin. Buprenorphine is effective in initiating acute withdrawal and suppressing withdrawal symptoms.

Alcohol Dependence. An example of another type of medication is one used to treat alcoholism: disulfiram. The basis for this agent's therapeutic effect is different from that of methadone or naltrexone. When someone is maintained on disulfiram, alcohol ingestion causes stomach distress and, possibly, vomiting because the disulfiram prevents the breakdown of a noxious alcohol metabolite by the liver. Patients maintained on disulfiram should come to forget the pleasant effects of alcohol use, which is similar to the psychological basis of naltrexone maintenance. Moreover, they should begin to develop an aversion to alcohol use. Another similarity to the use of naltrexone is that disulfiram treatment of alcoholism has not been very successful because the patient who wants to use alcohol again can simply stop using disulfiram.

Some pharmacological agents have been tested to reduce craving for alcohol and thus help the alcoholic abstain from drinking. As of 2008, there were four medications approved by the U.S. Food and Drug Administration for the treatment of alcohol dependence: disulfiram, naltrexone, acamprosate, and a long-acting injectable formulation of naltrexone. Naltrexone may be beneficial in preventing a return to heavy drinking because its effects, like those of most drugs of abuse, are believed to be mediated, in part, through the brain's natural opiate system (e.g., endorphins). Other medications that have been studied for treatment of alcohol dependence include serotonergic medications and anticonvulsants, including topiramate. However, as in the treatment of opiate abuse, alcoholics must be detoxified before any of these medications are used as maintenance agents.

Tobacco Dependence. One commonly used pharmacological treatment for tobacco dependence is nicotine gum (Nicorette). The main reason to quit smoking is that it is linked to lung cancer, emphysema, and other serious illnesses. Yet the active ingredient in cigarettes, nicotine, is associated with pleasant effects and with withdrawal discomfort, thereby making it an extremely addicting drug. Providing smokers with nicotine replacement in the form of a gum helps them avoid the health risks associated with cigarettes. One problem with nicotine gum is that it is difficult to chew correctly; people need to be shown how to chew it in order to get the therapeutic effect. A patch is also available that is placed on the arm and automatically releases nicotine. This method shows good treatment potential. Other forms of nicotine replacement therapy include: lozenges, inhalers, and nasal spray. The patch, gum, and lozenge are available for over-the-counter purchase.

The first non-nicotine treatment approved to treat nicotine dependence is the antidepressant bupropion. The medication varenicline also became available as an effective smoking cessation treatment. Bupropion may have beneficial effects by increasing availability of the neurotransmitter dopamine. Varenicline reduces craving and withdrawal symptoms following cessation or reduction in nicotine consumption. It also has been shown to reduce the satisfied feeling gained through smoking. Detoxification from nicotine may also be facilitated with the medication clonidine, the same agent used to help alleviate opiate withdrawal symptoms.

Stimulant Dependence. Developing pharmacological treatment agents for stimulant (e.g., cocaine) dependence is a difficult task but has been the focus of a great deal of research. One of the difficulties in treating cocaine abuse is that cocaine affects many different neurotransmitter systems in various ways. Thus one approach may be to develop a treatment drug or regimen of drugs that affects a variety of neurotransmitter systems. However, the exact nature of the neural effects of cocaine was not entirely understood as of 2008.

Another difficulty is that it is not clear what approach to take in developing a treatment drug. One obvious technique in developing a medication for cocaine abuse is to use an agent that blocks the rewarding aspects of cocaine use. This type of drug would, presumably, decrease cocaine use because the rewarding effects are no longer experienced. However, this approach is similar to having opiate addicts use naltrexone, which has not been well accepted by heroin addicts. Clinical work with some treatment agents that were suggested to block the rewarding effects of cocaine did not prove to be useful in the treatment of abuse and

dependence. Whether this lack of treatment effect resulted from a flaw in the method or from the limited knowledge of cocaine's effects on neurotransmitter systems is not clear. One problem is that the potential blocking agents for cocaine may produce dysphoria, or an unpleasant feeling.

Another approach to treating cocaine abuse and dependence is based on a premise similar to that of methadone for opiate abuse. That is, a pharmacological agent similar in its effects to cocaine, but one that is not addicting, may be a useful anticraving agent. Just as methadone helps alleviate drug withdrawal, an agent of this type for cocaine abuse may alleviate the distress and craving associated with abstinence from cocaine. Several medications of this type have been tried, including bromocriptine and amantadine. As of 2008, these and other agents have shown some limited treatment promise.

Most of the approaches to developing pharmacological treatments for cocaine abuse have been based on research suggesting that one specific neurotransmitter (dopamine) is important for cocaine's rewarding effects. Yet other neurotransmitters are activated during cocaine use and may be better targets for developing new treatment drugs. That is, although dopamine is critical for the rewarding aspects of cocaine use, other neurotransmitter systems may be more important in withdrawal distress. Although withdrawal distress from cocaine has been difficult to document, depression is thought to be one important consequence of abstaining from chronic cocaine use. Antidepressant medications, such as desipramine and imipramine, have shown limited treatment potential, as have some anticonvulsant medications (e.g., tiabapine and topiramate), antinarcoleptics (modafinil), and antihypertensives (selegiline).

Sedative Dependence. Treatments for sedative dependence as of 2008 include detoxification agents, not anticraving agents. Detoxification is accomplished by tapering the dosage of benzodiazepines over two to three weeks. Carbamazepine, an antiseizure analgesic medication, has shown promise in relieving sedative withdrawal symptoms. Future work with agents that block the actions of benzodiazepines may hold promise as a maintenance or anticraving agent to help the sedative abuser abstain from drug abuse.

Marijuana Dependence. Although marijuana is the most commonly used illicit drug in the United States, there are no FDA-approved medications for the treatment of cannabis dependence. Withdrawal symptoms, such as negative mood, muscle pain, chills, and weight loss following daily use of marijuana quite likely play a role in relapse to marijuana use and impede abstinence efforts. Antidepressants and other mood stabilizers, as well as oral THC (a cannabinoid agonist) have been tested in clinical studies to reduce withdrawal symptoms. However, marijuana dependence appears to be as difficult to treat as other drug dependence and thus other options are needed.

One of the great lessons learned from the practice of giving medications to drug-abusing individuals is that these medications must be accompanied by psychological and social treatments and support. Medications do not work by themselves. Moreover, medications that are developed based on principles of altering or blocking the drug's effects in the brain may not be useful in practice to treat drug abuse and dependence because the premises on which the pharmacological treatment was developed may not be valid. Yet the largest research challenge is to understand the etiology and mechanisms of drug abuse. Thus, more research in many fields is needed to identify potential medications in order to develop more effective treatments for the difficult problems of drug abuse and dependence.

See also **Addiction: Concepts and Definitions; Imaging Techniques: Visualizing the Living Brain.**

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DRUGS AS DISCRIMINATIVE STIMULI

Human behavior is influenced by numerous stimuli in the environment. Those stimuli acquire behavioral control when certain behavioral consequences occur in their presence. As a result, a particular behavioral response becomes more or less likely to occur when those stimuli are present. For example, several laboratory experiments have demonstrated that it is possible to increase a particular response during a stimulus (such as a distinctively colored light) by arranging for reinforcement (such as a preferred food or drink) to be given following that response when the stimulus is present; when that stimulus is absent, however, responses do not produce the reinforcer. Over a period of time, responding will then occur when the stimulus is present but not when it is absent. Stimuli that govern behavior in this manner are termed *discriminative stimuli* and have been widely used in behavioral and pharmacological research to better understand how behavior is controlled by various stimuli, and how those stimuli, in turn, might affect the activity of various drugs.

It is important to recognize that there are differences between discriminative stimuli that merely set the occasion for a response to be reinforced and other types of stimuli that directly *produce* or *elicit* responses. Discriminative stimuli do not coerce a response from the individual in the same way that a stimulus such as a sharp pierce evokes a reflexive withdrawal response. Instead, discriminative stimuli may be seen as providing guidance to behavior because of the unique history of reinforcement that has occurred in their presence.

DRUGS AS DISCRIMINATIVE STIMULI

Although the stimuli that typically govern behavior are external (i.e., located in the environment outside the skin), it is also possible for internal or subjective stimuli to influence behavior. One of the more popular methods to emerge in the field of behavioral pharmacology has been the use of drugs as discriminative stimuli. The procedure consists of establishing a drug as the stimulus, in the presence of which a particular response is reinforced. Typically, to establish a drug as a discriminative stimulus, a single dose of a drug is selected and, following its administration, one of two responses are reinforced; with rodents or nonhuman primates, this usually entails pressing one of two simultaneously available levers, with reinforcement being scheduled intermittently after a fixed number of correct responses. Alternatively, when saline or a placebo is administered, responses on the other device are reinforced. Over a number of experimental sessions, a discrimination develops between the administration of the drug and saline, with the interoceptive (subjective) stimuli produced by the drug seen as guiding or controlling behavior in much the same manner as any external stimulus, such as a visual or auditory stimulus. Once the discrimination has been established, as indicated by the selection of the appropriate response following either the training drug or the saline administration, it is possible to investigate aspects of the drug stimulus in the same way as one might investigate other physical stimuli. It is thus possible to determine gradients of intensity or dose-effect functions with the training drug as well as generalization functions aimed at determining how similar the training drug dose is to a different dose or to another drug substituted for the training stimulus.

BASIC EXPERIMENTAL RESULTS

One of the more striking aspects of the drug discrimination technique is the strong relationship that has been found between the stimulus-generalization profile and the receptor-binding characteristics of the training drug. For example, animals trained to discriminate between a benzodiazepine anxiolytic, such as chlordiazepoxide, and saline solution typically respond similarly to other drugs that also interact with the receptor sites for benzodiazepine ligands. Anxiolytic drugs that produce their effects through other brain mechanisms or receptors do not engender responses similar to those occasioned by benzodiazepines. This suggests that it is activity at a specific receptor that is established when this technique is used and not the action of the drug on a

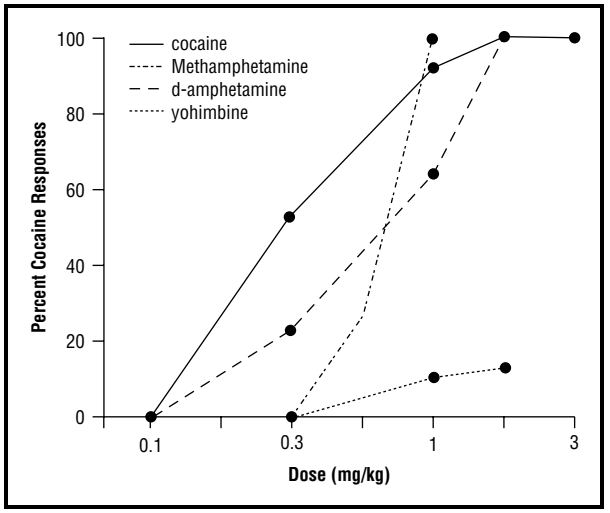

Figure 1. Discriminative stimuli. Effects of establishing a dose of 1.7 mg/kg cocaine, administered intramuscularly, as a discriminative stimulus in pigeons. Following the administration of the training dose of cocaine, 30 consecutive pecks on one illuminated response key resulted in food reinforcement, whereas following the administration of saline, 30 consecutive pecks on a different key produced food. Once the discrimination was established, various doses of other drugs were substituted for cocaine. The discriminative stimulus effects of cocaine were dose-dependent, with doses from 0.1 to 1.7 producing increases in responding on the key correlated with the training dose of cocaine. Similarly, d–amphetamine and methamphetamine also resulted in responding on the cocaine key, thereby showing that these drugs have some of the same subjective stimulus properties and presumably neuropharmacological effects as cocaine. A drug that does not produce generalization, yohimbine, an α2-adrenoreceptor antagonist, resulted only in modest levels of responding on the cocaine-associated response key, which suggests that this is not a mechanism by which cocaine produces its subjective behavioral and pharmacological effects. (Adapted from Johnson & Barrett, 1993.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

hypothetical psychological construct such as anxiety (Barrett & Gleeson, 1991).

Several studies have examined the effects of drugs of abuse by using the drug discrimination procedure, and they have established cocaine and numerous other drugs—such as an opiate, phencyclidine (PCP), or marijuana—as a discriminative stimulus in an effort to help delineate the neuropharmacological or brain mechanisms that contribute to the subjective and abuse-liability effects of these drugs. As an example, Figure 1 shows the results obtained in pigeons trained to discriminate a 1.7 milligram per kilogram (mg/kg) dose of cocaine from saline. The dose-response function demonstrates that doses below the training dose of cocaine yielded a diminished percentage of responses on the key correlated with cocaine administration, which suggests that the lower doses of cocaine were less discernible than the training dose. In addition, other psychomotor stimulants such as amphetamine and methamphetamine also produced cocaine-like responses, and this suggests that these drugs share some of the neurochemical properties of cocaine. In contrast, other drugs, such as the α_2-adrenoreceptor antagonist yohimbine, along with several other drugs such as morphine, PCP, or marijuana (that are not illustrated) do not produce responding on the key correlated with cocaine administration—thereby suggesting that the mechanisms of action underlying those drugs, as well as their subjective effects, are not similar to those of cocaine and the other psychomotor stimulants in this figure.

IMPLICATIONS

The use of drugs as discriminative stimuli has provided a wealth of information on the way drugs are similar to more conventional environmental stimuli in their ability to control and modify behavior. The procedure has also increased our understanding of the neuropharmacological mechanisms that operate to produce the constellation of effects associated with those drugs. The technique has wide generality and has been studied in several species, including humans—in whom the effects are quite similar to those of nonhumans.

Because it is believed that the subjective effects of a drug are critical to its abuse potential, the study of drugs of abuse as discriminative stimuli takes on added significance. A better understanding of the effects of drugs of abuse as pharmacologically subjective stimuli provides a means by which to evaluate possible pharmacological as well as behavioral approaches to the treatment of drug abuse. For example, a drug that prevents or antagonizes the discriminative-stimulus effects (and presumably the neuropharmacological actions) of an abused drug might be an effective medication to permit individuals to diminish their intake of abused drugs, because the stimuli usually associated with its effects will no longer occur. Similarly, although little work has been performed on the manipulation of environmental stimuli correlated with the drug stimulus, it might be possible to

design innovative treatment strategies in which other stimuli compete with the subjective discriminative-stimulus effects of the abused drug. Thus, a basic experimental procedure such as drug discrimination has provided a useful experimental tool for understanding the behavioral and neuropharmacological effects of abused drugs.

Further work may help design and implement novel treatment approaches to modifying the behavioral and environmental conditions surrounding the effects of abused drugs and thus result in diminished behavioral control by substances of abuse.

See also **Abuse Liability of Therapeutic Drugs: Testing in Animals; Drug Types; Research, Animal Model: An Overview.**

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June Stapleton

MEASURING EFFECTS OF DRUGS ON BEHAVIOR

People throughout the world take drugs such as heroin, cocaine, and alcohol because these drugs alter behavior. For example, cocaine alters general activity levels; it increases wakefulness and decreases the amount of food an individual eats. Heroin produces drowsiness, relief from pain, and a general feeling of pleasure. Alcohol's effects include relaxation, increased social interactions, marked sedation, and impaired motor function. For the most part, the scientific investigations of the ways drugs alter behavior began in the 1950s, when chlorpromazine was introduced as a treatment for schizophrenia. As a result of this discovery, scientists became interested in the development of new medications to treat behavioral disorders as well as in the development of procedures for studying behavior in the laboratory.

HOW IS BEHAVIOR STUDIED?

The simplest way to study the effects of drugs on behavior is to pick a behavior, give a drug, and observe what happens. Although this approach sounds very easy, the study of a drug's effect on behavior is not so simple. Like any other scientific inquiry, research in this area requires careful description of the behaviors being examined. If the behavior is not carefully described, it is difficult to determine whether a change in behavior following drug administration is actually due to the drug.

Behavior is best defined by describing how it is measured. By specifying how to measure a behavior, an *operational definition* of that behavior is developed. For example, to study the way in which a drug alters food intake, the following procedure might be used: First, select several people and present each with a box of cereal, a bowl, a spoon, and some milk after they wake up in the morning. Then measure how much cereal and milk they each consume within the next thirty minutes. To make sure the measurements are correct, repeat the observations several times under the same conditions (i.e., at the same time of day, with the same foods available). From these observations, determine the average amount of milk and cereal consumed by each person. This is the baseline level. Once the baseline level is known, give a small amount of drug and measure changes in the amount of milk and cereal consumed. Repeat the experiment, using increasing amounts of the drug. This concept of baseline level and change from baseline level is common to many scientific investigations.

In addition to defining behavior by describing how it is measured, a good behavioral procedure is also (1) sensitive to the ways in which drugs alter behavior and (2) is reliable. Sensitivity refers to whether a particular behavior is easily changed as the result of drug administration. For example, food consumption may be altered by using cocaine, but other behaviors may not be. Reliability refers to whether a drug produces the same effect each time it is taken. In order to say that cocaine reliably alters

the amount of food consumed, it should decrease food consumption each time it is given, provided that the experimental conditions surrounding its administration are the same.

WHAT FACTORS INFLUENCE A DRUG'S EFFECTS ON BEHAVIOR?

Although good behavioral procedures are necessary for understanding a drug's effects on behavior, pharmacological factors are also important determinants of a drug's effect. Pharmacological factors include the amount of drug given (the *dose*), how quickly the drug produces its effects (its *onset*), the time it takes for its effects to disappear (its *duration*), and whether the drug's effects are reduced (*tolerance*) or increased (*sensitivity*) if it is taken several times. Although this point may seem obvious, it is often overlooked. It is impossible to describe the behavioral effects of a drug on the basis of just one dose of the drug, since drugs can have very different effects, depending on how much of the drug is taken. Moreover, the probability that a drug will produce an effect also depends on the amount taken. As an example, consider Figure 1, which shows the risk of being involved in a traffic accident as a function of the amount of alcohol in a person's blood.

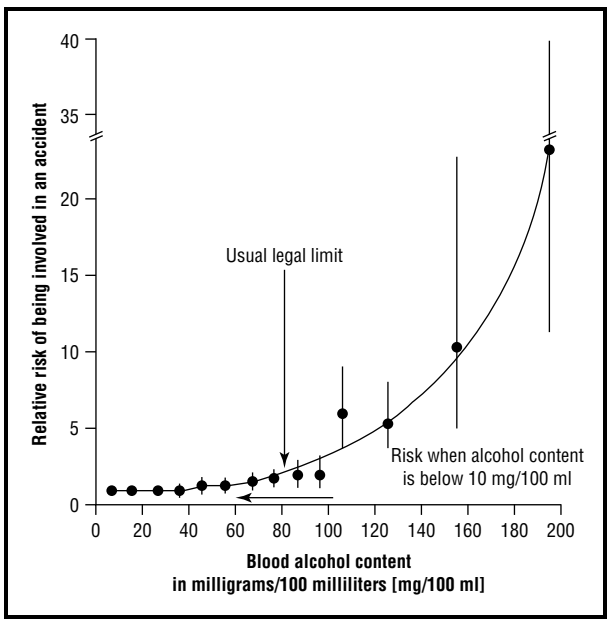

Figure 1. Risk of being involved in a traffic accident as a function of the amount of alcohol in the blood. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The way in which a drug is taken is also important. Cocaine can be taken by injection into the veins, by smoking, or by sniffing through the nose. Each of these routes of administration can produce different effects. Environmental factors also influence a drug's effect. Cocaine might change the amount of cereal and milk consumed in the morning but it might not change the amount consumed at a different time of day or if other types of food are available. Finally, individual factors also influence the drug effect. These include such factors as how many times an individual has taken a particular drug; what happened the last time it was taken; or what one may have heard from friends about a drug's effects.

HOW IS BEHAVIOR STUDIED IN THE LABORATORY?

Human behavior is very complex, and it is often difficult to examine. Although scientists do conduct studies on people, many investigations of drug effects on behavior are carried out using animals. With animals, investigators have better control over the conditions in which the behavior occurs as well as better information about the organism's past experience with a particular drug. Although animal experiments provide a precise, controlled environment in which to investigate drug effects, they also have their limitations. Clearly, they cannot research all the factors that influence human behavior. Nevertheless, many of the effects that drugs produce on behavior in animals also occur in humans. Moreover, behavioral studies sometimes require a large number of subjects with the same genetic makeup or with no previous drug experience. It is easier to meet these requirements in animal studies than in studies with people.

Since animals are often used in research studies, it is important to remember that behavioral scientists are very concerned about the general welfare of their animals. The U.S. Animal Welfare Act set standards for handling, housing, transporting, feeding, and veterinary care of a wide variety of animals. In addition, all animal research in the United States is now reviewed by a committee that includes a veterinarian experienced in laboratory-animal care. This committee inspects animal-research areas and reviews the design of experiments to ensure that the animals are treated well.

WHAT APPROACHES ARE USED TO EXAMINE DRUG EFFECTS?

In general, there are two ways to examine drug effects on behavior in the laboratory. One approach relies on observation of behavior in an animal's home cage or in an open area in which the animal (or person) can move about freely. When observational approaches are used, special precautions are necessary. First of all, the observer's presence should not disrupt the experiment. Television-monitoring systems and videotaping make it possible for the observer to be completely removed from the experimental situation. Second, the observer should not be biased. The best way to ensure that the observer is not biased is to make the observer "blind" to the experimental conditions; that is, the observer does not know what drug is given or which subject received the drug. If the study is done in human subjects, then they also should be blind to the experimental conditions. An additional way to make sure observations are reliable is to use more than one observer and compare observations. If these precautions are taken, observational approaches can produce interesting and reliable data. Indeed, much of what is known about drug effects on motor behavior, food or water intake, and some social behaviors comes from careful observational studies.

Another approach uses the procedures of classical and operant conditioning. This involves training animals to make specific responses under special conditions. For example, in a typical experiment of this sort, a rat is placed in an experimental chamber and trained to press a lever to receive food. The number and pattern of lever presses are measured with an automatic device, and changes in responding are examined following drug administration. These procedures have several advantages. First, they produce a very consistent measure of behavior. Second, they can be used with human subjects as well as with several different animal species. Third, the technology for recording behavior eliminates the need for a trained observer.

WHAT BEHAVIORS DO DRUGS ALTER?

Some of the behaviors that drugs alter are motor behavior, sensory behavior, food and water intake, social behavior, and behavior established with classical and operant conditioning procedures. By combining investigations of these behaviors, scientists classify drugs according to their prominent behavioral effects. For example, drugs such as amphetamine and cocaine are classified as psychomotor stimulants because they increase alertness and general activity in a variety of different behavioral procedures. Drugs such as morphine are classified as analgesics because they alter the perception of pain, without altering other sensations such as vision or audition (hearing).

Motor Behavior. Most behaviorally active drugs alter motor behavior in some way. Morphine usually decreases motor activity, whereas with cocaine certain behaviors occur over and over again (that is, repetitively). Other drugs, such as alcohol, may alter the motor skills used in driving a car or operating various types of machinery. Finally, some drugs alter exploratory behavior, as measured by a decrease in motor activity in an unfamiliar environment. Examination of the many ways in which drugs alter motor behavior requires different types of procedures. Some of these procedures examine fine motor control or repetitive behavior; others simply measure spontaneous motor activity.

Although changes in motor behavior can be observed directly, most studies of motor behavior use some sort of automatic device that does not depend on human observers. One of these devices is the running wheel. The type of running wheel used in scientific investigations is similar to the running wheel in pet cages. This includes a cylinder of some sort that moves around an axle when an animal walks or runs in it. The only difference between a running wheel in a pet cage and a running wheel in the laboratory is its size and the addition of a counter that records the number of times the wheel turns. Another device for measuring motor behavior uses an apparatus that is surrounded by photocells. If the animal moves past one of the photocells, a beam of light is broken and a count is produced. Yet another way to measure motor behavior is with video tracking systems. An animal is placed in an open area and a tracking system determines when movement stops and starts as well as its speed and location. This system provides a way to look at unique movement patterns such as repetitive behaviors. For example, small amounts of amphetamine increase forward locomotion, whereas larger amounts produce repetitive behaviors such as head bobbing, licking, and rearing. Until recently, this type of repetitive behavior was measured by direct observation and description.

Percent blood alcohol	Behavioral effect
0.05	alertness reduced
0.10	reaction time prolonged
0.20	motor function impaired
0.30	severe motor impairment
0.40	consciousness lost

Table 1. Blood alcohol level and behavioral effect. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Although technology for measuring motor behavior is very advanced, it is important to remember that how much drug is given, where it is given, and the type of subject to whom it is given will also influence a drug's effect on motor behavior. Whether a drug's effects are measured at night or during the day is an important factor. The age, sex, species, and strain of the animal is also important. Whether food and water are available is another consideration as well as the animal's previous experience with the drug or test situation. As an example, see Table 1, which shows how the effects of alcohol on motor behavior differ depending on the amount of alcohol in a person's blood.

Sensory Behavior. The integration and execution of every behavior an organism engages in involves one or more of the primary senses, including hearing, vision, taste, smell, and touch. Obviously, a drug can affect sensory behavior and thereby alter a number of different behaviors. For example, drugs such as lysergic acid diethylamide (LSD) produce visual abnormalities and hallucinations. Phencyclidine (PCP) produces a numbness in the hands and feet. Morphine alters sensitivity to painful stimuli.

It is difficult to investigate drug effects on sensory behavior, since changes in sensory behavior cannot be observed directly. In order to determine whether someone hears a sound, one must report having heard it. In animal studies, rats or monkeys are trained to press a lever when they hear or see a given stimulus. Then a drug is given and alterations in responding are observed. If the drug alters responding, it is possible that the drug did so by altering sensory behavior; however, care must be taken in coming to this conclusion since a drug might simply alter the motor response used to measure sensory behavior without changing sensory behavior at all.

One area of sensory behavior that has received considerable attention is pain perception. In most procedures for measuring pain perception, a potentially painful stimulus is presented to an organism and the time it takes the organism to respond to that stimulus is observed. Once baseline levels of responding are determined and considered reliable, a drug is given. If the time it takes the organism to respond to the stimulus is longer following drug administration and if this change is not because the animal is too sedated to make a response, then the drug probably has altered pain perception.

Among the most common procedures used to measure pain perception is the tail-flick procedure in which the time it takes an animal to remove its tail from a heat source is measured prior to and after administration of a drug such as morphine. Another commonly used procedure measures the time it takes an animal to lick its paws when placed on a warm plate or to remove its tail from a container of warm water. Thus, an alteration in pain perception is operationally defined as a change in responding in the presence of a painful stimulus. It is also important to note that the animal, not the experimenter, determines when to respond or remove its tail. Also, these procedures do not produce long-term damage or discomfort that extends beyond the brief experimental session.

Food and Water Intake. The simplest way to measure food and water intake is to determine how much an organism eats or drinks within a given period of time. A more thorough analysis might also include counting the number of times an organism eats or drinks in a single day, or measuring the time between periods of eating and periods of drinking. Several factors are important in accurately measuring food and water intake. For example, how much food or water is available to the organism and when is it available? Is it a food the organism likes? When did the last meal occur?

In animals, food intake is often measured by placing several pieces of pelleted food of a known weight in their cages. The food that remains after a period of time is weighed and subtracted from the original amount to get an estimate of how much was actually eaten. Water intake is usually measured with calibrated drinking tubes clipped to the front of the animal's cage or with a device called a

drinkometer, which counts the number of times an animal licks a drinking tube. An accurate measure of fluid intake also requires a careful description of the surrounding conditions. For example, was fluid intake measured during the day or during the night? Was food also available? What kind of fluid was available? Was there more than one kind of fluid available? These procedures are also used to examine drug intake. If rats are presented with two different drinking tubes, one with alcohol, another with water, they will generally drink more alcohol than water; however, the amount they drink is generally not sufficient to produce intoxication or physical dependence. Rats will drink a large amount of alcohol as well as other drugs of abuse such as morphine and cocaine when these drugs are the only liquid available. Indeed, most animals will consume sufficient quantities to become physically dependent on alcohol or morphine.

Social Behavior. Behaviors such as aggression, social interaction, and sexual behavior are usually measured by direct experimenter observation. Aggressive behavior can be measured by observing the number of times an animal engages in attack behavior when another animal is placed into its cage. In some cases, isolation is used to produce aggressive behavior. Sexual behavior is also measured by direct observation. In the male rat or cat, the frequency of behaviors such as mounting, intromission, and ejaculation are observed. Another interesting procedure for measuring social behavior is the social interaction test. In this procedure, two rats are placed together and the time they spend in active social interaction (sniffing, following, grooming each other) is measured under different conditions. In one condition, the rats are placed in a familiar environment; in another condition, the environment is unfamiliar. Rats interact more when they are in a familiar environment than when they are in an unfamiliar environment. Moreover, antianxiety drugs increase social interaction in the unfamiliar area. These observational techniques can produce interesting data, provided that they are carried out under well-controlled conditions, the behavior is well-defined, and care is taken to make sure the observer neither disrupts the ongoing behavior nor is biased.

Classical Conditioning. Classical conditioning was made famous by the work of the Russian scientist Ivan Pavlov in the 1920s. In those experiments, Pavlov used the following procedure. First, dogs were prepared with a tube to measure saliva, as shown in Figure 2. Then Pavlov measured the amount of saliva that was produced when food was given. The amount of saliva not only increased when food was presented but also when the caretaker arrived with the food. From these careful observations, Pavlov concluded that salivation in response to the food represented an inborn, innate response that did not require any learning. Because no learning was required, he called this an unlearned (unconditioned) response and the food itself an unlearned (unconditioned) stimulus. The dogs did not automatically salivate, however, when the caretaker entered the room; but after the caretaker and the food occurred together several times, the presence of the caretaker was paired with (or conditioned to) the food. Pavlov called the caretaker the *conditioned stimulus* and he called the salivation that occurred in the presence of the caretaker a *conditioned response.*

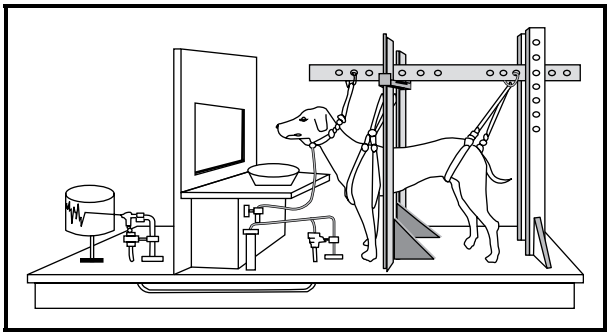

Figure 2. Diagram of Pavlov's classical conditioning experiment. A tube is attached to the dog's salivary duct, and saliva drops into a device that records the number of drops. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Events in the environment that are paired with or conditioned to drug delivery can also produce effects similar to the drug itself, much in the same way that Pavlov's caretaker was conditioned to food delivery. For example, when heroin-dependent individuals stop taking heroin, they experience a number of unpleasant effects, such as restlessness, irritability, tremors, nausea, and vomiting. These are called withdrawal or abstinence symptoms. If an individual experiences withdrawal several times in the same

environment, then events or stimuli in that location became paired with (or conditioned to) the withdrawal syndrome. With time, the environmental events themselves can produce withdrawal-like responses, just as the caretaker produced salivation in Pavlov's dogs.

Operant Conditioning. About a decade after Pavlov's discovery of classical conditioning, another psychologist, B. F. Skinner, was developing his own theory of learning. Skinner observed that certain behaviors occur again and again. He also observed that behaviors with a high probability of occurrence were behaviors that produced effects on the environment. According to Skinner, behavior "operates" on the environment to produce an effect. Skinner called this process *operant conditioning*. For example, people work at their jobs because working produces a paycheck. In this situation, working is the response and a paycheck is the effect. In other situations, a person does something to avoid a certain effect. For example, by driving a car within the appropriate speed limit, traffic tickets are avoided and the probability of having a traffic accident is reduced. In this case, the response is driving at a given speed and the effect is avoiding a ticket or an accident.

If the effect that follows a given behavior increases the likelihood that the behavior will occur again, then that event is called a *reinforcer*. Food, water, and heat are common reinforcers. Drug administration is also a reinforcer. It is well known that animals will respond on a lever to receive intravenous injections of morphine, cocaine, and amphetamine, as well as a number of other drugs. Not all drugs are self-administered, however. For example, animals will respond to avoid the presentation of certain nonabused drugs such as the antipsychotics (medications used in the treatment of schizophrenia). Because there is a good correlation between drugs that are self-administered by animals and those that are abused by people, the self-administration procedure is often used to examine drug-taking behavior.

In most operant conditioning experiments, animals perform a simple response such as a lever press or a key peck to receive food. Usually the organism has to make a fixed number of responses or to space responses according to some temporal pattern. The various ways of delivering a reinforcer are called *schedules of reinforcement*. Schedules of reinforcement produce very consistent and reliable patterns of responding. Moreover, they maintain behavior for long periods of time, are easily adapted for a number of different animals, and provide a very accurate measure of behavior. Thus, they provide a well-defined, *operational measure* of behavior, which is used to examine the behavioral effects of drugs.

Motivation, Learning, Memory, and Emotion. One of the biggest challenges for behavioral scientists is to develop procedures for measuring drug effects on processes such as motivation, emotion, learning, or memory since these behaviors are very difficult to observe directly. Drugs certainly alter processes such as these. For example, many drugs relieve anxiety. Other drugs produce feelings of pleasure and well-being; still others interfere with memory processes. Given the complexity of devised procedures, they are not described in detail here; however, it is important to emphasize that the approach for examining the effects of drugs on these complex behaviors is the same as it is for any behavior: First, carefully define the behavior and describe the conditions under which it occurs. Second, give a drug and observe changes in the behavior. Third, take special care to consider pharmacological factors, such as how much drug is given, when the drug is given, or the number of times the drug is given. Fourth, consider behavioral factors, such as the nature of the behavior examined, the conditions under which the behavior is examined, as well as the individual's past experience with the behavior.

RESEARCH: MEASURING EFFECTS OF DRUGS ON BEHAVIOR: SUMMARY

To find out how drugs alter behavior, several factors are considered. These include the pharmacology of the drug itself as well as an understanding of the behavior being examined. Indeed, the behavioral state of an organism, as well as the organism's past behavior and experience with a drug contribute as much to the final drug effect as do factors such as the dose of the drug and how long it lasts. Thus, the examination of drug effects on behavior requires a careful description of behavior with special attention to the way in which the behavior is measured. Behavioral studies also require a number of experimental controls, which assure that changes in behavior following drug administration are actually due to the drug itself and not the result of behavioral variability.

See also **Addiction: Concepts and Definitions; Aggression and Drugs: Research Issues; Pharmacodynamics; Psychomotor Effects of Alcohol and Drugs; Reinforcement; Research, Animal Model: An Overview; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Sensation and Perception and Effects of Drugs; Tolerance and Physical Dependence.**

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LINDA A. DYKSTRA

MEASURING EFFECTS OF DRUGS ON MOOD

Subjective effects are feelings, perceptions, and moods that are the personal experiences of an individual. They are not accessible to other observers for public validation and, thus, can only be obtained through reports from the individual. Subjective-effect measures are used to determine whether the drug is perceived and to determine the quantitative and qualitative characterization of what is experienced. Although subjective effects can be collected in the form of narrative descriptions, standardized questionnaires have greater experimental utility. For example, they may be used to collect the reports of individuals in a fashion that is meaningful to outside observers, can be combined across subjects, and can provide data that are reliable and replicable. The measurement of subjective effects through the use of questionnaires is scientifically useful for determining the pharmacologic properties of drugs—including time course, potency, abuse liability, side effects, and therapeutic utility. Many of the current methods used to measure subjective effects resulted from research aimed at reducing drug abuse.

HISTORY

Drug abuse and drug addiction are problems that are not new to contemporary society; they have a long-recorded history, dating back to ancient times. For centuries, various drugs including alcohol, tobacco, marijuana, hallucinogens, opium, and cocaine, have been available and used widely across many cultures. Throughout these times, humans have been interested in describing and communicating the subjective experiences that arise from drug administration. Although scientists have been interested in the study of pharmacology for many centuries, reliable procedures were not developed to measure the subjective effects of drugs until recently.

Throughout the twentieth century, the U.S. Government has become increasingly concerned with the growing problem of drug abuse. To decrease the availability of drugs with significant abuse liability, the government has passed increasingly restrictive laws concerning the possession and sale of existing drugs and the development and marketing of new drugs. The pressing need to regulate drugs that have potential for misuse prompted the government to sponsor research for the development of scientific methodologies that would be useful in assessing the abuse liability of drugs.

Two laboratories that made major contributions to the development of subjective-effect measures were Henry Beecher and his colleagues at Harvard University and the government-operated Addiction Research Center (ARC) in Lexington, Kentucky. Beecher and his colleagues at Harvard conducted a lengthy series of well-designed studies that compared the subjective effects of various drugs—opiates, sedatives, and stimulants—in a variety of subject populations that included patients, substance abusers, and normal volunteers and highlighted the importance of studying the appropriate patient population. Additionally, this

group laid the foundation for conducting studies with solid experimental designs, which include double-blind and placebo controls, randomized dosing, and characterization of dose-response relationships. Investigators at the ARC conducted fundamental studies of both the acute (immediate) and chronic (long-term) effects of drugs, as well as physical dependence and withdrawal symptoms (e.g., Himmelsbach's opiate withdrawal scale). A number of questionnaires and procedures now in use to study the subjective effects of drugs were developed, including the Addiction Research Center Inventory and the Single Dose Questionnaire. Although many of the tools and methods developed at the ARC are still in use, other laboratories have since modified and expanded subjective-effect measures and their applications.

MEASURES

Question Format. Subjective-effects measures are usually presented in the form of groups of questions (questionnaires). These questions can be presented in a number of formats, the most frequently used of which are ordinal scales and visual analog scales. The ordinal scale is a scale of ranked values in which the ranks are assigned based upon the amount of the measured effect that is experienced by each individual. Subjects are usually asked to rate their response to a question on a 4- or 5-point scale (e.g., to rate the strength of the drug effect from 0 to 4, with 0 = not at all; 1 = a little; 2 = moderately; 3 = quite a bit; and 4 = extremely). A visual-analog scale is a continuous scale presented as a line without tick marks or sometimes with tick marks to give some indication of gradations. A subject indicates the response by placing a mark on that line, according to a particular reference point; for example, lines are usually anchored at the ends with labels such as "not at all" and "extremely." Visual-analog scales can be unipolar (example: "tired," rated from no effect to extremely), or they may be bipolar (example: "tired/alert," with "extremely tired" at one end, "extremely alert" at the other, and "no effect" in the center). Another frequently used format is the binomial scale, usually in the form of yes/no or true/false responses, such as the Addiction Research Center Inventory. A fourth format utilizes a nominal scale, in which the response choices are categorical in nature and mutually exclusive of each other (e.g., drug class questionnaire).

Questionnaires. Frequently used subjective-effect measures include investigator-generated scales, such as adjective-rating scales, and standardized questionnaires, such as the Profile of Mood States and the Addiction Research Center Inventory. A description of a number of questionnaires follows; however, this list is illustrative only and is not meant to be exhaustive.

Adjective Rating Scales. These are questionnaires on which subjects rate a list of symptoms, describing how they feel or effects associated with drug ingestion. The questionaires can be presented to subjects with either visual-analog or ordinal scales. Items can be used singly or grouped into scales. Some adjective-type scales are designed to measure global effects, such as the strength of drug effects or the subject's liking of a drug, while other adjective rating scales are designed to measure specific drug-induced symptoms. In the latter use, the adjectives used may depend on the class of drugs being studied and their expected effects. For example, studies of amphetamine include items such as "stimulated" and "anxious," while studies of opioids include symptoms such as "itching" and "talkative." To study physical dependence, symptoms associated with drug withdrawal are used; for example, in studies of opioid withdrawal, subjects might rate "watery eyes," "chills," and "gooseflesh." Most adjective-rating scales have not been formally validated; investigators rely on external validity.

Profile of Mood States (POMS). This questionnaire was developed to measure mood effects in psychiatric populations and for use in testing treatments for psychiatric conditions such as depression and anxiety. It is a form of an adjective-rating scale. This scale was developed by Douglas McNair, Ph.D., and has been modified several times. It exists in two forms—one consisting of sixty-five and another of seventy-two adjectives describing mood states that are rated on a five-point scale from "not at all" (0) to "extremely"

(4). The item scores are weighted and grouped by factor analysis into a number of subscales, including tension-anxiety, depression-dejection, anger-hostility, vigor, fatigue, confusion-bewilderment, friendliness, and elation. This questionnaire has been used to measure acute drug effects, usually by comparing measures collected before and after drug administration. Its use in drug studies has not been formally validated; however, it has been validated by replication studies in normal and psychiatric populations and in treatment studies.

Single Dose Questionnaire. This was developed in the 1960s at the ARC to quantify the subjective effects of opioids. It has been used extensively and has been modified over time. This questionnaire consists of four parts; (1) a question in which subjects are asked whether they feel a drug effect (a binomial yes/no scale); (2) a question in which subjects are asked to indicate which among a list of drugs or drug classes is most similar to the test drug (a nominal scale); (3) a list of symptoms (checked yes or no); and (4) a question asking subjects to rate how much they like the drug (presented as an ordinal scale). The list of drugs used in the questionnaire includes placebo, opiate, stimulant, marijuana, sedative, and other. Examples of symptoms listed are turning of stomach, skin itchy, relaxed, sleepy, and drunken. While this questionnaire has not been formally validated, it has been used widely to study opioids, and the results have been remarkably consistent over three decades.

Addiction Research Center Inventory (ARCI). This is a true/false questionnaire containing more than 550 items. The ARCI was developed by researchers at the ARC to measure a broad range of physical, emotive, and subjective drug effects from diverse pharmacological classes. Subscales within the ARCI were developed to be sensitive to the acute effects of specific drugs or pharmacological classes (e.g., morphine, amphetamine, barbiturates, marijuana); feeling states (e.g., tired, excitement, drunk); the effects of chronic drug administration (Chronic Opiate Scale); and drug withdrawal (e.g., the Weak Opiate Withdrawal and Alcohol Withdrawal Scale). The ARCI subscales most frequently used in acute drug-effect studies are the Morphine-Benzedrine Group (MBG) to measure euphoria; the Pentobarbital-Chlorpromazine-Alcohol Group (PCAG) to measure apathetic sedation; and the Lysergic Acid Diethylamide Group (LSDG) to measure dysphoria or somatic discomfort. The use of the MBG, PCAG, and LSDG scales has remained standard in most studies of abuse liability. Subscales on this questionnaire were developed empirically, followed by extensive validation studies.

Observer-rated Measures. These may frequently accompany the collection of subjective effects and are often based on the subjective-effect questionnaires. Ratings are made by an observer who is present with the subject during the study, and items are limited to those drug effects that are observable. Observer-rated measures may include drug-induced behaviors (e.g., talking, scratching, activity levels, and impairment of motor function), as well as other drug signs such as redness of the eyes, flushing, and sweating. Observer-rated measures can be designed using any of the formats used in subject-rated measures. Examples of observer-rated questionnaires that have been used extensively are the Single Dose Questionnaire, which exists in an observer-rated version, and the Opiate Withdrawal Scale developed by Himmelsbach and his colleagues at the ARC.

USES OF SUBJECTIVE-EFFECT MEASURES

The methodology for assessing the subjective effects of drugs was developed, in large part, to characterize the abuse liability, the pharmacological properties, and the therapeutic utility of drugs. *Abuse liability* is the term for the likelihood that a drug will be used illicitly for nonmedical purposes. The assessment of the abuse-liability profile of a new drug has historically been studied by comparing it with a known drug, whose effects have been previously characterized. Drugs that produce euphoria are considered more likely to be abused than drugs that do not produce euphoria.

Subjective-effects measures may also be used to characterize the time course of a drug's action (such

	Global effects	ARCI	POMS	Adjectives
Sedatives	Drug effect Liking High	PCAG	Fatigue (increase) Vigor (decrease)	Tired Sleepy Relaxed Drunk
Stimulants	Drug effect Liking High	MBG	Vigor (increase) Fatigue (decrease)	Stimulated Nervous Thirsty Jittery
Opiates	Drug effect Liking High	MBG PCAG		Nauseous Itchy Nodding Energetic

Table 1. Typical response profiles for sedatives, stimulants, and opiates on selected subjective-effect measures. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

as time to drug onset, time to maximal or peak effect, and the duration of the drug effect). These procedures can provide information about the pharmacological properties of a particular drug, such as its drug class, whether it has agonist or antagonist effects, and its similarity to prototypic drugs within a given drug class. Subjective-response reports are also useful in assessing the efficacy (the ability of a drug to produce its desired effects), potency (amount or dose of a drug needed to produce that effect), and therapeutic utility of a new drug. Subjective reports provide information regarding the potency and efficacy of a new drug in comparison to available treatment agents. Subjective-effect measures may be useful in determining whether a drug produces side effects that are dangerous or intolerable to the patient. Drugs that produce unpleasant or dysphoric mood-altering effects may have limited therapeutic usefulness.

DESCRIPTION OF MAJOR FINDINGS OBTAINED WITH DIFFERENT DRUG CLASSES

Drugs of different pharmacological classes generally produce profiles of subjective effects that are unique to that class of drugs and that are recognizable to individuals. The subjective effects of major pharmacological classes have been characterized using the questionnaires described above. Table 1 lists some major pharmacological classes and their typical effects on various instruments. While global measures provide quantitative information regarding drug effects, they tend not to differentiate among different types of drugs. Nevertheless, the more specific subjective-effect measures, such as the ARCI and the Adjective Rating Scales, yield qualitative information that can differentiate among drug classes.

RESEARCH: MEASURING EFFECTS OF DRUGS ON MOOD: CONCLUSION

Measures of the subjective effects of drugs have been extremely useful in the study of pharmacology. Questionnaires have been developed that are sensitive to both the global effects and the specific effects of drugs; however, research is still under way to develop even more sensitive subjective-effect measures and new applications for their use.

See also **Addiction: Concepts and Definitions; Drug Types; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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MOTIVATION

Motivation is a theoretical construct that refers to the neurobiological processes responsible for the initiation and selection of such goal-directed patterns of behavior

as are appropriate to the physiological needs or psychological desires of the individual. *Effort* or *vigor* are terms used to describe the intensity of a specific pattern of motivated behavior. Physiological "drive" states, caused by imbalances in the body's homeostatic regulatory systems, are postulated to be major determinants of different motivational states. Deprivation produced by withholding food or water is used routinely in studies with experimental animals to establish prerequisite conditions in which nutrients or fluids can serve as positive reinforcers in both operant and classical conditioning procedures. In more natural conditions, the processes by which animals seek, find, and ingest food or fluids are divided into appetitive and consummatory phases. Appetitive behavior refers to the various patterns of behavior that are used to locate and bring the individual into direct contact with a biologically relevant stimulus such as water. Consummatory behavior describes the termination of approach behavior leading subsequently to ingestion of food, drinking of fluid, or copulation with a mate.

Incentive motivation is the term applied to the most influential psychological theory that explains how the stimulus properties of biologically relevant stimuli, and the environmental stimuli associated with them, control specific patterns of appetitive behavior (Bolles, 1972). According to this theory, the initiation and selection of specific behaviors are triggered by external (incentive) stimuli that also guide the individual toward a primary natural incentive, such as food, fluid, or a mate. Drugs of abuse and electrical brain-stimulation reward can serve as artificial incentives. In a further refinement of this theory, Berridge and Valenstein (1991) defined incentive motivation as the final stage in a three-part process. The first phase involves the activation of neural substrates for pleasure, which in the second phase are associated with the object giving rise to these positive sensations and the environmental stimuli identified with the object. The critical third stage involves processes by which salience is attributed to subsequent perceptions of the natural incentive stimulus and the associated environmental cues. It is postulated that this attribution of "incentive salience" depends upon activation of the mesotelencephalic dopamine systems. The sensation of pleasure and the classical associative learning processes that mediate stages one and two respectively are subserved by different neural substrates.

In the context of drive states as the physiological substrates of motivation, the level of motivation is manipulated by deprivation schedules in which the subject is denied access mainly to food or water for fixed periods of time (e.g., 22 hours of food deprivation). An animal's increased motivation can be inferred from measures such as its running speed in a runway to obtain food reward. Under these conditions, speed is correlated with level of deprivation. Another measure of the motivational state of an animal is the amount of work expended for a given unit of food, water, or drug. Work here is defined as the number of lever presses per reinforcer. If one systematically obtains an increase in the number of presses, one can identify a specific ratio of responses per reward beyond which the animal is unwilling to work. This final ratio is called the break point. In the context of drug reinforcement, the break point in responding for cocaine can be increased or decreased in a dose-dependent manner by dopamine agonists and antagonists respectively.

Appetitive behavior also can be measured directly in animal behavior studies either by an animal's latency (the time it takes) in approaching a source of food or water during presentation of a conditioned stimulus predictive of food, or simply by measuring the animal's latency approaching a food dispenser when given access to it. The fact that these appetitive behaviors are disrupted by dopamine antagonists has been interpreted as evidence of the role of mesotelencephalic dopamine pathways in incentive motivation.

In extending these ideas to the neural bases of drug addiction, Robinson and Berridge (1993) emphasized the role of sensitization, or enhanced behavioral responses to fixed doses of addictive drugs, that occurs after repeated intermittent drug treatment. Neurobiological evidence indicates that sensitization is directly related to neuroadaptations in the mesotelencephalic dopamine systems. As a result of these neural changes, a given dose of amphetamine, for example, causes enhanced levels of extracellular dopamine and an increase in the behavioral effects of the drug. Given the role proposed for the mesotelencephalic dopamine systems in incentive salience, it is further conjectured that craving, or exaggerated desire for a specific object or its mental representation, is a direct result of drug-induced sensitization. In this manner, repeated self-administration of drugs of

abuse, such as amphetamine, produce neural effects that set the stage for subsequent craving for repeated access to the drug.

See also **Brain Structures and Drugs; Research, Animal Model: An Overview; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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ANTHONY G. PHILLIPS

RESEARCH, ANIMAL MODEL: AN OVERVIEW.

Since the 1970s, research using experimental animals has made major contributions to understanding the etiology of drug abuse. Indeed, one can view the sequence of historical development of this knowledge as paralleling much of what now appears to be the sequence of the development of addiction. That sequence is:

1. Assessment of the rewarding nature of the drug upon initial intake.
2. Possible sensitization of the drug effect with continued intake.
3. Linking of the drug reward to originally neutral external stimuli.
4. Addiction, or compulsive drug-taking.

The following review will examine the history of this research and present the current consensus view of the etiology of drug abuse, with particular reference to landmark studies with experimental animals. First, however, a few comments on terminology are in order.

Experimental analyses of drug effects on behavior began in laboratories using the methods of operant, or instrumental, conditioning. Early investigators not only used the methods of operant conditioning, they also adopted the terminology of operant conditioning, which developed in the 1920s and dominated American psychology until the end of the 1960s. To illustrate, this terminology can be applied to a situation of acquisition in which the pressing of a lever results in intravenous delivery of a drug to a rat. First, the rat would spontaneously *emit* movements, or *responses*, some of which would include lever-presses. If each lever-press resulted in the intravenous injection of the drug, and if the frequency of lever pressing increased over time, the drug would be called a *positive reinforcer*. Notice that there is no statement about the rat "liking" the drug. In fact, the word *reward* was not used to describe the drug because, as originally used by Thorndike (1911), that term referred to a "satisfying state of affairs." The language of operant conditioning, in an attempt to be more scientific, would not refer to the unknown internal state of the rat.

If one asked an investigator using the terminology of operant conditioning why the rat self-administered the drug, the investigator would say that because the rate of lever-pressing increased once the drug infusion was made contingent upon the response, the drug must, by definition, be a positive reinforcer. This approach was, of course, criticized as being a tautology. Why was the drug a positive reinforcer? Because delivery of it contingent upon a response resulted in an increase in the occurrence of that response. Why did the responding increase? Because the drug was a positive reinforcer.

In an odd way, the operant view of drug addiction coincided with the medical view of drug addiction during the same historical period. The medical view said very little about the etiology of addiction. Rather, a person simply became an addict (perhaps because of a weak will) and was then physically dependent on the drug (defined by the occurrence of somatic withdrawal signs when the drug was discontinued). The problem was how to get the person to stop taking the drug. In the medical view, drug taking was maintained by avoidance of the aversive state of withdrawal. The operant conditioning approach to this view was that drug taking was maintained by *negative reinforcement*; that is, the response of drug administration removed the noxious state of withdrawal.

The conceptual and semantic worlds of the operant conditioning laboratory and the medical clinic were similar in emphasizing the behavior of the addict and saying little about the internal state of the addict. Those worlds began to change as a result of an experiment reported in 1954.

THE IDEA OF A REWARD SYSTEM IN THE BRAIN

Olds and Milner reported in 1954 that rats would press levers to deliver brief electrical stimulation to electrodes chronically implanted in their brains. They named the phenomenon intracranial self-stimulation (ICSS). Studies in the ensuing 15 years mapped the brains of rats and other animals for ICSS and found the greatest response rates and lowest current thresholds to be in the posterior hypothalamus and ventral midbrain regions. Stein (1964) found that experimenter-administered amphetamine potently increased ICSS responding, and Crow (1972) reported high rates of responding from electrodes in the region of the dopaminergic cell bodies of the ventral midbrain. By 1982 the "dopamine hypothesis" of ICSS reward, and indeed all reward, had been proposed (Wise, 1982). This hypothesis was particularly attractive because it explained not only ICSS, but psychostimulant reward as well, in terms of a single brain "reward system." Note that with the entry of more neuroscience-oriented research, the term *reward* began to be used interchangeably with, or instead of, *positive reinforcement.*

The discovery of ICSS led to the idea of a brain reward system being the substrate of drug reward and drug abuse. The earlier emphasis on the behavior of the addict as an attempt to stave off withdrawal was replaced with a view of addictive behavior as being based on the hedonic value of the drug.

ASSESSING DRUG REWARD IN EXPERIMENTAL ANIMALS

The argument is often made that if a drug increases ICSS responding, or particularly if it decreases the current threshold for ICSS, that drug will most likely be a drug of abuse. This procedure, however, does not directly measure the reward of the drug itself. Instead, it assesses the modulatory effect of the drug on a separate rewarding stimulus, the electrical stimulation of the brain. Thus, procedures that more directly measure the reward of the drug must be viewed as being closer to the world of the human drug addict. Two procedures are commonly used to assess the reward value of a drug in experimental animals: conditioned place preference (CPP), which is almost exclusively used with rat subjects, and intravenous self-administration (IVSA), which is used with rats and, to a more limited extent, with monkeys.

Conditioned Place Preference (CPP). Conditioned place preference utilizes classical (Pavlovian) conditioning. In the simplest version, the rat is placed in a chamber divided into two easily discriminable compartments that differ in the brightness of the walls, the texture of the floor, and sometimes in their odor. Ideally, in the initial 15-minute test, the rat will not evince a preference for either compartment. On subsequent training sessions, the rat is injected with the drug of interest or the drug vehicle and confined in one of the compartments, typically for 30 minutes. One compartment is paired with the drug for two to four sessions, and the other compartment is paired with the vehicle for two to four sessions (typically these alternate). Finally, in the test session, the rat is allowed to freely move about the chamber without having been injected before the session. If the rat spends more time in the drug-paired chamber than the vehicle-paired chamber (compared with pre-drug testing), the drug is declared to be rewarding. If the rat avoids the drug-paired chamber, the drug is deemed aversive.

CPP has various benefits. It is easy to do, for one thing, and many animals and drugs can be tested in this way. It also has limitations, however. First, humans typically administer a drug to themselves, even the first time they try it. While the classical conditioning aspect of CPP clearly happens in humans—as in the case of the "needle freak," for whom the act of intravenous injection is rewarding—the fact is that after initial use, both the addict-to-be and the addict seek out the drug. Second, the single, rather crude measure of time in the drug-associated compartment does not provide much in the way of the "texture" of behavior. Regardless, this approach has been very widely used.

Intravenous Self-Administration (IVSA). Intravenous self-administration (IVSA), in contrast, utilizes

operant (instrumental) conditioning. A catheter is implanted into a vein (usually the jugular) of the rat, leading to a port on the animal's head or back. After minimal initial training using food reward, the rat is allowed to press a lever or "nose-poke" (into a hole in the wall, breaking a light beam) to activate a syringe pump that delivers a fixed amount of drug solution into the vein via the catheter. Work with monkeys has the advantage of more available veins (typically in the back); the monkey wears a vest covering the catheter.

In the simplest version of IVSA, each response results in a drug infusion. This is a fixed-ratio 1 (FR1) schedule of reinforcement. In an attempt to generate more behavior to better examine the effect of a manipulation on the drug taking, the schedule may be shifted to a partial reinforcement version. For the FR schedule, this might be FR2, FR4, and so on. Many studies have been done examining the effect of difference schedules of reinforcement (FR, variable-interval, fixed-interval, etc.) on drug-reinforced responding. The use of schedules in which the drug is not delivered upon each lever-press is thought to better measure the reinforcing or rewarding value of the drug, and thus may be closer to a human's "craving" for the drug.

Perhaps the major difficulty with the IVSA procedure is in the interpretation of the results. If a manipulation (e.g., brain lesion, systemic drug injection, social deprivation) results in an increased rate of IVSA of a drug, does that mean the drug has become more or less rewarding? An increase in the dose per injection of most drugs of abuse results in a lower response rate by the animal. A decrease in the dose per injection results in a higher response rate. The interpretation is that the animal is titrating the concentration of drug in the bloodstream—too low is not rewarding enough, and too high is aversive. Therefore, if a manipulation decreases the response rate, that manipulation has probably increased the reward of the drug.

This explanation is mostly likely accurate using an FR1 schedule, in which each response delivers the drug. The use of a partial reinforcement schedule of drug delivery may make it more difficult for the animal to achieve the desired blood level, and thus the incentive value of the drug rises in importance. A commonly used method to decrease the role of the response rate in IVSA is to use a progressive-ratio (PR) schedule of reinforcement. In this procedure, a trained animal must meet the criterion of a progressively increasing response requirement (e.g., the exponential series 1, 2, 4, 6, 9, 12, . . . 251, 331 . . .) within a self-administration session. The variable of interest is the "breakpoint," or when the animal ceases to complete a ratio requirement. Higher breakpoints are interpreted as indicating a higher reward value for the drug.

The IVSA procedure has its benefits. One can test the animal over and over again, varying the conditions (dose, presence of other drugs, etc.), and it is the method most similar to the human situation, in which people actively seek out and self-administer the drug. However, it also presents a major challenge in that it is difficult to do—the catheter must be flushed with an anticoagulant to prevent clogging, the animal must not overdose, and infections can be a worry. In general, drugs that produce a CPP are drugs that support IVSA. There are exceptions, but more agreements than exceptions.

A DOPAMINE SYSTEM AS THE BASIS OF PSYCHOSTIMULANT DRUG REWARD

Studies using CPP and IVSA conducted between 1975 and 1985 rapidly accumulated evidence that the neurotransmitter dopamine is crucial to psychostimulant (amphetamines and cocaine) reward. Systemic injection of dopamine receptor antagonists reduced the efficacy of psychostimulants to produce a CPP. Low doses of dopamine receptor antagonists increased the rate of IV self-administration of psychostimulants. The increased responding was interpreted as a compensatory response for the decreased reward, and high doses of the same antagonists decreased or abolished responding. Increased responding at low doses was crucial, because high doses of these antagonists induce a Parkinson's-like state, (Parkinson's disease is largely caused by degeneration of dopamine-releasing neurons in the brain), obscuring whether the reduced responding at high doses was due to blunted reward or motor impairment.

Soon after the demonstrations using systemically administered antagonists, the question was asked: Which dopamine system? Chemical neuroanatomists had defined a number of dopamine-using sets of neurons in the mammalian brain. Two prominent systems, containing approximately 95 percent of total brain dopamine, were identified. Both have neuronal cell bodies located in the mesencephalon

(*midbrain* in English) and terminals in the forebrain. One is the *nigrostriatal* system, with cell bodies in the substantia nigra pars compacta and dopamine-releasing terminals in the dorsal striatum (composed of the caudate and putamen nuclei in primates, but fused as a caudate-putamen in rodents). Sometimes the nigrostriatal system is referred to as the *mesostriatal* system. The second is the mesocorticlimbic system, with cell bodies in the ventral tegmental area of Tsai (VTA) and major terminal fields in the nucleus accumbens septi and prefrontal cortex. This entry will term these subdivisions of the mesocorticolimbic system the *mesoaccumbens* and *mesofrontal* systems, respectively.

The studies to answer the question of which dopamine system is involved were all carried out using rats, due to the numbers of subjects needed and the necessity of intracranial manipulations, which are more difficult in primates. Selective destruction of the nigrostriatal system was achieved using intra-nigral injections of the neurotoxin 6-hydroxydopamine (6-OHDA). For anatomical reasons, midbrain injections of 6-OHDA could not be used to destroy the mesocorticolimbic system (they would also damage the nigrostriatal system), so injections were made into the forebrain terminal fields.

Studies using CPP and IVSA of psychostimulants agreed that the nigrostriatal and mesofrontal dopamine systems did not seem necessary for the rewarding effect, and that the mesoaccumbens system seemed crucial for the reward effect. These results converged with another, much less used, approach, in which rats self-administered amphetamine solution in extremely small volumes directly into the nucleus accumbens but not into the dorsal striatum. Finally, additional work, using CPP with both 6-OHDA and intracerebral injection, indicated that another, smaller dopamine system originating in the VTA and terminating in the ventral pallidum formed a *mesopallidal* reward system for psychostimulant reward (Gong et al., 1996a).

INDIVIDUAL DIFFERENCES IN PSYCHOSTIMULANT REWARD

For any drug of abuse, a minority of those sampling it move on to addiction. By the beginning of the 1990s, it was clear that while considerable progress had been made in determining the neurochemical and neuroanatomical bases of psychostimulant reward, possible neurobiological bases of individual differences in the development of addiction were unknown. Work with humans over a number of decades had resulted in numerous debates over postulated "addictive personalities," but work with nonhuman animals had been scarcely investigated.

A paper by Piazza and colleagues, published in 1989, initiated studies on an animal model of differences in addiction vulnerability that continue to the present. These investigators screened rats for their locomotor response to a novel environment (an activity-measuring chamber where the rats had never been). Using a median split, they separated the rats into high-responder (HR) and low-responder (LR) groups. When these rats were subsequently implanted with IV catheters and allowed to nose-poke respond for injections of a low dose of amphetamine, the HR rats acquired self-administration but the LR rats did not.

The debate about why humans are attracted to psychostimulants goes back decades. Some assume that these individuals are basically depressed and taking the drug to elevate their mood (self-medicate), while others believe them to be "sensation-seekers," for whom the drug emulates the biological state accompanying "thrills." The results of Piazza and colleagues were interpreted as being consistent with the "thrill-seeking" or "sensation-seeking" argument.

A steady production of research results by the Piazza group and others has clarified the nature of the HR-LR difference. The Piazza group found the elevation of the "stress hormone" corticosterone (the primate version is cortisol) by a mild stressor lasted longer in HR than LR rats. They also reported that HR, but not LR, rats would intravenously self-administer corticosterone. This finding, which does not appear to have been replicated, is nonetheless consistent with a large literature indicating that elevated corticosterone, whether induced via injection or stressor, enhances self-administration of psychostimulants (Goeders, 2003). This work is very exciting because it opens up the possibility that humans under stressful environmental conditions (e.g., poverty) are more responsive to the rewarding effect of psychostimulants, and thus more likely to become addicted.

Some peculiarities of the HR-LR difference may shed further light on the nature of the difference. First, although a number of laboratories have replicated the faster acquisition of IVSA of psychostimulants by

HR rats compared to LR rats, those who have used the CPP method have not found an HR-LR difference for amphetamine (Erb & Parker, 1994) or cocaine (Gong et al., 1996b). Second, a critical article by Mitchell and colleagues (2005) reported that while HR rats acquired lever-pressing at a higher rate with IV cocaine or food pellets, and that while this rate correlated with their locomotor activity in a novel environment, the correlation between locomotion and responding for cocaine disappeared if the rats were pretrained to lever-press for food. This seemed to show that in a free-operant procedure without pre-exposure to the apparatus, HR rats acquire lever-pressing for cocaine at a faster rate simply because they are more active in novel environments, not because the reward of the cocaine is greater than in LR rats.

As noted by Marinelli (2005), the procedure used by Mitchell and colleagues was unusual. They used a very brief (15 minute) locomotor screening (the usual is 30–120 minutes), and acquisition of lever-pressing was done with an FR5 schedule (the usual is FR1). Furthermore, studies have shown HR-LR differences in psychostimulant IVSA after acquisition, and that HR rats previously trained on FR1 will respond more than LR rats on a progressive-ratio schedule (Grimm & See, 1997).

Another unusual observation is that when IVSA of psychostimulants in HR and LR rats is compared across a range of doses, the usual "inverted-U" dose-response curve is seen, but it is displaced upward in the HR relative to the LR rats (Piazza et al., 2000; Belin et al., 2008). The expectation is that if HR rats are more sensitive to the reward of psychostimulants, their dose-response curve should be shifted to the left of that of the LR rats. Instead, it is shifted vertically. The interpretation of the vertical shift has been contentious.

Aspects of behavioral differences in HR and LR rats in nondrugged conditions may afford some insight into the above peculiarities of the HR-LR difference. In particular, HR rats seem to find novel environments less aversive. Kabbaj and colleagues (2000), using standard rodent tests of anxiety and fear, found HR rats to be less fearful than LR rats. Presumably, this is why they show more locomotor activity in a novel environment. Decades of work with rats has indicated that locomotor activity in a novel environment is determined by the competing tendencies to explore the environment or to withdraw for safety. One can interpret the higher locomotor activity of the HR rats as a heightened tendency to explore or a decreased tendency to withdraw.

The French group who originally described the HR/LR distinction has leaned toward the heightened tendency to explore (the "sensation-seeking" argument previously described), suggesting that the stress of the novel environment triggers the release of corticosterone, and that corticosterone is rewarding in HR rats (Piazza & Le Moal, 1996). On the other hand, Kabbaj and colleagues (2000) found less messenger RNA (mRNA) for corticotrophin-releasing hormone (CRH) in the central nucleus of the amygdala and less mRNA for the CRH receptor in the hippocampus of HR rats as compared to LR rats. CRH was first discovered as a chemical signal released by the hypothalamus. This signal travels via vasculature to activate the release of adrenocorticotrophic releasing hormone by the pituitary; the pituitary signal then evokes the release of corticosterone into the general circulation. However, CRH is also a transmitter, released within the brain by some cells, which acts via CRH receptors on other neurons. Because an extensive literature relates amygdala activity to fear and anxiety, a lower number of CRH receptors in the amygdala of HR rats is consistent with the idea that although HR rats may show a greater corticosterone response in the blood to stress, they may also show a lower activation of brain systems for fear and anxiety than LR rats.

Psychostimulants are well known to produce anxiety—even panic—in a subset of people who take them. A series of experiments by Ettenberg has measured this in rats. Rats are trained to traverse an alley where the reward at the end is an intravenous or intracerebroventricular (into the brain ventricular system) infusion of cocaine. Ettenberg's group (e.g., Guzman & Ettenberg, 2007) found that, with both routes of administration, higher doses of the drug cause the animals to exhibit approach-avoidance behavior, which they can measure.

The vertical shift in the psychostimulant dose-response curves seen in HR rats may be a consequence

of their having less of an anxiety component in their response to these drugs than do LR rats. Indeed, this may be a major part of why they more rapidly acquire psychostimulant IVSA than LR rats.

SENSITIZATION

It has been known for a very long time that repeated administration of many psychoactive drugs results in tolerance, or a progressive decrease in response to a drug. Human abusers of psychostimulants and opiates can eventually consume quantities that would be lethal for nontolerant users. Thus, it was a great surprise when it was reported that repeated administration of amphetamine to rats resulted in a progressively greater increase in locomotor activity and stereotyped behaviors. Initially termed *reverse tolerance*, this phenomenon has now become known as *sensitization* (Stewart & Vezina, 1988; Everitt & Wolf, 2002). As will be subsequently examined, the neural mechanisms of sensitization have been intensively investigated. However, for understanding the relevance of this work to human drug abuse, the question of whether sensitization occurs for the rewarding effect of a drug is crucial.

It is virtually impossible to investigate possible sensitization of drug reward using humans. To do such a study, a group of people not previously exposed to the drug would be repeatedly administered the drug, and the psychological and behavioral effects would be investigated in a longitudinal fashion. For both ethical and legal reasons this cannot be done, and one must look to research with other animals. The closest approximation in work with humans has been investigations of paranoid thinking induced by psychostimulants, which has been reported to show sensitization (e.g. Bartlett et al., 1997).

Experimenter-delivered pre-exposure to cocaine facilitates the acquisition of IVSA (Schenk & Partridge, 2000) and increases breakpoints on a progressive ratio schedule (Covington & Miczek, 2001). Work from the laboratory of D. C. S. Roberts (Morgan et al., 2006) has investigated sensitization in rats using self-administered cocaine. In their procedure, rats were given access to cocaine by insertion of a response lever into the test chamber once every 15 minutes. A lever-press resulted in a single drug infusion followed by retraction of the lever. This procedure was in place 24 hours a day (the rats lived in the test chambers) for 10 consecutive days, followed by 7 days of forced abstinence. No lever was present during the period of abstinence. The advantage of this method was that, unlike previous experiments in which the animal was allowed access 24 hours a day, drug intake could be limited to avoid the signs of toxicity noted with the previous approach. When the animals were retested on a progressive ratio schedule using cocaine self-administration after the abstinence period, the breakpoint of responding was greatly increased. Roberts and colleagues interpreted these results as modeling the "binge-abstinence" pattern of cocaine administration seen in human users, and they noted the resulting sensitization.

Neurobiological work has been carried out with the goal of determining the cellular and molecular mechanisms of psychostimulant sensitization. Virtually all of this work has involved the most easily measured behavioral effects of locomotor activity and stereotypy (continuous repetition of a particular action). Locomotor activity is typically measured via a chamber with infrared light beams, which are invisible to the rat, crossing just above the floor. Advanced software can measure not only the number of beams broken by the rat's locomotion, but the sequence of beam breaks, allowing determination of the animal's path. This is particularly important if stereotypy is involved, because then the rat locomotes relatively little, typically staying in one region of the chamber to lick an area, gnaw the floor, or some similar action. Locomotor activity is a low-dose phenomenon and stereotypy is a high-dose phenomenon.

Induction of sensitization can be carried out in various ways. One method is to inject the animal with a constant dose every few days and measure the resulting increase in locomotion or stereotypy. Another is to administer a constant or escalating dose for a number of consecutive days, stop administration, then measure the locomotion or stereotypy at a later time (e.g., a week later). In all cases, the behavioral response to the drug increases.

The psychostimulants amphetamine and cocaine increase transmission for the monoaminergic transmitters dopamine, norepinephrine, and serotonin. Studies in the 1970s using receptor antagonists revealed that the increased locomotion and stereotypy produced by psychostimulants is largely due to the effect on dopamine. This was followed by work

to determine which sets of dopaminergic terminals were responsible. Studies using local brain injections of dopamine receptor antagonists, selective neurotoxins, and amphetamine and cocaine themselves led to the conclusion that the locomotor effect of psychostimulants is caused by increased dopaminergic transmission in the ventral pallidum—and particularly in the nucleus accumbens—whereas the stereotypy is caused by similar transmission in the dorsal striatum.

Not surprisingly, sensitization of the locomotor effect of psychostimulants seems to take place within the system originating in the VTA and terminating in the nucleus accumbens. Sensitization of the stereotypic effect seems to take place within the system originating in the SNPC and terminating in the dorsal striatum. Most studies have involved measuring locomotor activity, because this can readily be done using automated equipment.

The major questions, of course, have been: "Where in each system does sensitization occur?" and "What is the mechanism of this sensitization?" We will consider the *mesoaccumbens* component of the mesocorticolimbic system, with locomotor activity as the measure. The development of sensitization can be blocked by the systemic administration of drugs that are antagonists at the N-methyl-D-aspartic acid (NMDA) subtype as well as the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) subtype of receptor for the neurotransmitter glutamate. These results indicate a significant involvement of glutamate in the phenomenon. A considerable amount of experimental evidence has implicated glutamatergic synapses in the regions of the dopaminergic cell bodies in the midbrain, particularly in the VTA. These results include: (1) injection of NMDA receptor antagonists into the VTA does not affect the locomotor response to systemically administered amphetamine, but it does prevent amphetamine sensitization from occurring, (2) injection of AMPA agonists into the VTA produces sensitization even though the rat has not previously been exposed to amphetamine, and (3) intra-VTA injection of a drug that facilitates the action of glutamate at NMDA receptors sensitizes rats to amphetamine. Other chemicals also seem to be involved. The "stress hormone" corticosterone is reported to enhance amphetamine sensitization via an action on glutamate transmission. Dopamine, released from dendrites of VTA neurons, appears to act via the D1 subtype of dopamine receptor to facilitate, via glutamate, amphetamine sensitization within the VTA.

Putting the above together, the current thinking is that stress, whether via the environment or a psychostimulant, elevates circulating corticosterone, and, with dopamine within the VTA, brings about a lasting facilitation at glutamatergic synapses on VTA dopaminergic neurons. This lasting facilitation is manifest as sensitization.

Considerable work at the cellular level supports the hypothesis that psychostimulant sensitization utilizes an extremely well-studied mechanism of synaptic plasticity called *long-term potentiation*, or *LTP*. The most basic LTP mechanism works in the following way. Transmission at a glutamatergic synapse acts on the AMPA subtype of glutamate receptor to depolarize the cell. If stronger depolarization occurs, either via a transient greater glutamate release or via another transmitter acting on the same cell, a simultaneous action of glutamate at a glutamate receptor of the NMDA subtype opens a channel in the cell membrane allowing the entry of calcium into the cell. The calcium cannot enter unless the membrane has been sufficiently depolarized by the action at the AMPA (which mimics effects of glutamate) or nonglutamate receptor. Entry of the calcium triggers an intracellular cascade of biochemical reactions, resulting in the insertion of more AMPA receptors than before into the cell membrane. These AMPA receptors remain, and glutamatergic transmission at that synapse is strengthened, meaning that a given amount of glutamate now results in greater membrane depolarization than before.

The LTP mechanism, or variants on it, are currently considered the best candidates for the mechanism of long-term or permanent memory at the cellular level. Just as it has been proposed that the rewarding effect of psychostimulants may result from a "hijacking" of the brain mechanisms for natural reward, it has been proposed that sensitization to psychostimulants may result from a hijacking of the cellular mechanisms for memory formation (see Hyman et al., 2006; Kaver & Malenka, 2007).

It has also been proposed that the glutamate in the VTA which effects LTP may be released by an axonal projection from the prefrontal cortex to the VTA or by another set of neurons that, activated by

the prefrontal cortex, release glutamate upon the VTA. Studies in rats have shown that electrical stimulation of the prefrontal cortex induces firing of VTA neurons via glutamate release upon the VTA, and that glutamate release in the VTA is greatly increased by psychostimulant administration. A number of research papers from different laboratories have reported that surgical damage to the prefrontal cortex greatly reduces or abolishes psychostimulant sensitization of locomotor activity in rats (e.g., Cador et al., 1999). It has also been reported that electrical stimulation of the prefrontal cortex induces sensitization in the absence of prior drug exposure.

RELAPSE

Relapse is one of the major, or perhaps *the* major, problem of drug addiction. Many therapies have been developed to treat addiction, but in the end, the value of most is diminished by extremely high rates of relapse. Work with experimental animals has shown that neutral stimuli can be paired with a drug, and that, via classical conditioning, those stimuli can evoke drug-taking, even if the drug-taking response has been extinguished. This can be seen if the drug is paired with stimuli or if withdrawal from the drug is paired with stimuli. After significant advances during the 1970s and 1980s in understanding the rewarding nature of many drugs of abuse, and after advances in the 1980s and 1990s concerning sensitization, work with experimental animals in the 1990s began to concentrate on the relapse phenomenon, particularly the neurobiological correlates.

Work with rats clearly shows three classes of stimuli that trigger the relapse of drug-taking behavior: (1) re-exposure to the drug, (2) presentation of stimuli previously associated with the drug, and (3) stress (Shaham et al., 2003).

Relapse Caused by Drug Re-exposure. In work from the laboratory of Dr. Jane Stewart (Mueller & Stewart, 2000), it has been shown that a conditioned place preference (CPP) to an environment paired with intraperitoneally administered cocaine can be reactivated after extinction via a cocaine injection. These investigators noted the surprising robustness of the CPP, which endured for weeks after conditioning, and the ease with which a single cocaine injection reactivated the CPP. This work is an example of relapse induced by contextual cues, although it was not known which of the many cues (brightness of wall, texture of floor, etc.) was linked to the drug state.

Dr. Peter Kalivas and colleagues have consistently used the intravenous self-administration procedure to examine relapse. In Kalivas's method, rats are trained to self-administer cocaine intravenously, and then subjected to response extinction by replacing the drug solution with saline. After responding is reduced to 10 percent or less of the drug-responding level for three sessions, a cocaine-priming dose is administered intraperitoneally before a session and responding with saline infusions is measured. A marked increase in responding typically results, which is viewed as a relapse.

A series of studies by Kalivas and colleagues has revealed the brain system necessary for this model of relapse. The method of finding the system consisted of the intracranial injection of a drug cocktail of GABA (gama-amino-butyric acid, the major inhibitory transmitter in the brain) agonists, which transiently suppresses neural activity in the injected region, just before the intraperitoneal administration of cocaine. The results of this method have shown that inactivation of the more dorsal components of the medial prefrontal cortex, the core of the nucleus accumbens, and the ventral pallidum substantially suppresses relapse responding. In other studies, this group has shown that the cocaine-priming dose induces glutamate release in the nucleus accumbens, and that this effect is decreased by inactivation of the medial prefrontal cortex. In addition, intra-accumbens administration of an antagonist for the AMPA, but not the NMDA, subtype of glutamate receptor suppresses relapse responding. Kalivas and colleagues explain all of the above by a model in which the activation of prefrontal neurons induces glutamate release in the core of the nucleus accumbens, which then effects relapse responding via an output to the ventral pallidum.

Interestingly, the Kalivas group has not found that antagonism of dopamine receptors in the nucleus accumbens prevents relapse responding. They suggest that cocaine-priming affects the prefrontal cortex, which then—via a glutamate signal—affects the accumbens. Furthermore, they report that the rise in extracellular glutamate in the

accumbens is only seen in animals that lever-press in the relapse test. Yoked controls that have not been trained to lever-press show a rise in accumbal dopamine in response to the relapse-inducing cocaine injection, but they do not exhibit a rise in glutamate.

Perhaps the most surprising result of the findings of Kalivas and colleagues is that the anatomical system necessary for cocaine relapse seems only partially responsible for the reward of the drug. Rats will more readily self-inject cocaine into the shell than the core of the accumbens. But relapse involves the core, not the shell. Damage to the medial prefrontal cortex of rats results in more robust responding, with higher breakpoints, for cocaine than is normally seen, yet this damage reduces cocaine-primed relapse. Finally, if one hypothesizes that the priming injection produced a state similar to that of self-administration, and thus results in a return of extinguished responding, the expectation would be that antagonism of dopamine, not glutamate receptors, in the accumbens would reduce relapse responding, and that prefrontal inactivation would be ineffective. However, the experimental results seem to be the opposite of this expected result.

One interpretation is that, rather than inducing a drug state that acts as a reminder, cocaine-priming affects a system for "impulse control." An enormous literature, stretching back decades, has implicated the prefrontal cortex in impulse control, and now it is receiving attention in human cocaine addicts (e.g., Ray Li et al., 2008). Norepinephrine and dopamine are both released within the prefrontal cortex, and that transmission should be enhanced by psychostimulants. Indeed, this is perhaps the dominant hypothesis at present to account for why psychostimulants such as amphetamine and methylphenidate are useful in the treatment of Attention-Deficit Disorder (ADD) and Attention-Deficit Hyperactivity Disorder (ADHD). Poor impulse control is a major component of these disorders. Kalivas and colleagues have found that an injection of a broad-spectrum dopamine antagonist into the prefrontal cortex blocks relapse due to cocaine re-exposure.

Relapse Caused by Drug-Associated Cues. There are of two types of drug-associated cues: discrete cues, such as a sound or light, and contextual cues, such as a test chamber. In humans, the discrete cues are thought to correspond to drug paraphernalia, while the contextual cues are thought to correspond to location. In this view, both kinds of cues evoke a "craving" state and lead to relapse.

The most straightforward way to model cue-evoked relapse is to pair the cue or cues with drug administration, institute a number of extinction sessions in which responses are ineffective or result in the delivery of saline until responding is very low, then subsequently examine the ability of the cue or cues to evoke responding. When this has been done, the results show that the presentation of a light or sound associated with drug infusion evokes responding (or relapse). On the neurobiological side, lesions of the basolateral amygdala (BLA) were reported to abolish the ability of the cues to evoke relapse. This is consistent with a large literature, particularly from fear conditioning, showing the role of the BLA in the linkage of a neutral stimulus with an emotional state. Transient inactivation of the rostral BLA has been found to be more effective in blocking cue-induced reinstatement than inactivation of the caudal BLA (Kantak et al., 2002). Given that the rostral BLA sends axons to the core of the accumbens (discussed above as being crucial for drug-induced reinstatement), cue-induced reinstatement may, in the end, activate the same subcortical system as drug-induced reinstatement.

It has been suggested that dopamine receptors of the D1 subtype within the BLA are important, because intra-BLA injection of a D1 (but not D2) antagonist blocks the reinstatement of responding by a drug-associated cue. These results are consistent with the finding that dopamine release increases in the BLA upon presentation of a drug-associated cue. Interestingly, BLA injections of antagonists at glutamate receptors (of both the AMPA and NMDA subtypes) are ineffective in affecting cue-evoked reinstatement. Much of the above is reviewed by Kalivas and McFarland (2003).

A much more limited number of experiments indicate that environmental context is linked to the drug state via the hippocampus, specifically the dorsal hippocampus. The hippocampus is an ancient cortex, pushed into a subcortical location by the growth of neocortex. An extremely extensive literature relates hippocampal function to spatial memory, and perhaps contextual memories in general, in rats. In humans, the hippocampus seems necessary for the formation of "declarative" memories, which are accessible to conscious retrieval. Inactivation of the

dorsal hippocampus, but not the basolateral amygdala, impairs reinstatement of cocaine self-administration in rats. The hippocampus sends axonal projections to the nucleus accumbens, particularly the shell component, so it reproduces the amygdalo-accumbens projection, while presumably carrying contextual rather than cue-related information.

Relapse Caused by Stress. The primary method used in these studies has been to train the rat to self-administer cocaine intravenously, then institute an extinction procedure for a number of sessions until responding is very low, and then administer an inescapable electric shock to the floor beneath the rat's feet (footshock). The result is a robust reinstatement of responding.

The brain systems involved in stress-evoked reinstatement seem to be different from those of drug-evoked and cue-evoke reinstatement (McFarland et al., 2004). Within the amygdala, the central nucleus (CeA), not the BLA, seems important. Transient inactivation of the CeA, or pharmacological blockade of receptors for norepinephrine in it, attenuate stress-evoked reinstatement. These findings make sense, because stressors increase the release of norepinephrine within the amygdala. The bed nucleus of the stria terminalis (BNST) is another forebrain structure that receives a norephinephrine-releasing input, and for which there is a large literature relating it to stress. Consistent with this, pharmacological blockade of noradrenergic receptors of the *beta* subtype in the BNST attenuates stress-induced reinstatement. Finally, an axonal projection from the CeA to the BNST is known to release the stress-associated peptidergic transmitter corticotropin-releasing hormone (CRH), and antagonism of CRH receptors in the BNST attenuates stress-induced relapse.

Comparison of the Neurobiology of Drug-, Cue-, and Stress-Evoked Relapse. While there is some overlap, the apparently distinct nature of the neural pathways for the three methods of inducing relapse is notable, at least for cocaine. Drug-induced relapse appears to depend on a circuit originating in the medial prefrontal cortex, projecting to the core of the accumbens, and thence to the ventral pallidum. The projection from cortex to accumbens utilizes glutamate as the transmitter and acts via the AMPA subtype of receptor in the accumbens. The amygdala does not seem particularly involved in this type of relapse. Cue-evoked relapse appears to depend on a circuit for which the basolateral amygdala is a central component. A glutamate-releasing projection from the BLA to the accumbens core is very important for this form of relapse, suggesting that, in the end, cue-evoked relapse activates the same "downstream" circuitry as drug-evoked relapse. Finally, the major components of stress-evoked relapse include the central nucleus of the amygdala and the bed nucleus of the stria terminalis. Release of norepinephrine in both structures, and the peptide CRH in the bed nucleus, appears crucial for stress-evoked relapse.

DRUG-ASSOCIATED STIMULI AS REWARDS

A considerable amount of work—rather than testing relapse directly—has been done to measure the ability of drug-related stimuli to maintain responding in the absence of the drug. It is thought that this taps into the mechanism of relapse, even though relapse itself is not tested.

Psychologists have a long history of talking about operant (instrumental) conditioning in two ways. On the one hand, when a stimulus follows a behavior and increases the probability of that behavior, that stimulus is, ipso facto, a positive reinforcer. On the other hand, the same stimulus can be considered as having "incentive" properties, thus energizing further responding. The "reinforcement" view emphasizes the ability of the stimulus to "stamp in" a response. The "incentive" view emphasizes the ability of the stimulus to facilitate additional responding, even for behaviors that did not precede the stimulus (e.g., exploration). Incentive-oriented theorists think the ability of a drug-associated stimulus to induce "craving" reflects an incentive-motivational property of the stimulus.

A theoretical paper on the neural basis of drug craving, written by Terry Robinson and Kent Berridge and published in 1993, has had a major impact on the incentive-oriented approach to drug addiction—and indeed on drug addiction studies in general. Basing their thinking largely on experimental and neurobiological studies with nonhuman animals, Robinson and Berridge considered both the negative reinforcement (escape from the aversion of withdrawal) and positive reinforcement approaches

to drug addiction, and they found both approaches wanting. Instead, they proposed that incentive salience (the attractiveness of stimuli linked to a drug via conditioning) is the basis of addiction. Of particular importance, they propose that the incentive properties of these stimuli sensitize with continued drug use. That is, they take the thinking about sensitization and extend it from the drug itself to stimuli associated with the drug. Robinson and Berridge conclude that, in the truly addicted individual, the incentive of the drug is maximum, while the actual reward experienced when the drug is consumed may be much lower than upon initial intake.

In a subsequent paper of Berridge's concerning food reward, published in 1996, he posited two processes, which he termed *liking* and *wanting*. Applied to drugs, *liking* means "On a 1 to 10 scale, how much did you like the drug?" and *wanting* means "How much do you want to consume the drug in the future?" Liking is very similar to *reward*, as it is typically thought of, and wanting is very similar to *incentive motivation*. The beauty of these terms, and the reason for their subsequent popularity, lies in the fact that these are everyday terms, not traditional psychological terms, and are thus easily understood.

Robinson and Berridge revisited their theory in 2003 in a paper in which they reviewed their ideas and incorporated intervening developments, including liking and wanting. They explicitly proposed that the core of drug addiction is the sensitization of the "wanting" system, which they had previously identified as being centered on the nucleus accumbens. Finally, they incorporated inhibitory control mechanisms, particularly prefrontal, which may be altered—even at the level of the morphology of single neurons—into their theory.

While not necessarily adopting the theoretical view of Robinson and Berridge, other researchers have presented compelling evidence for the importance of conditioned stimuli in maintaining drug consumption. In particular, work from the laboratories of Barry Everitt and Trevor Robbins, who often publish together, has advanced this knowledge. They have concentrated on using second-order schedules of reinforcement (reviewed in Di Ciano and Everitt, 2005). In this procedure, the drug (most often cocaine) is delivered via IV injection upon a lever-press. However, the press that delivers the drug is only part of a long chain of presses. For instance, in an FR10 (FR10:S) schedule, ten presses result in a brief illumination of a light ("S") that has been previously paired with IV cocaine injection. However, nine such "units" of responding are necessary before the completion of the tenth produces a cocaine injection. In the even more stringent FI15 (FR10:S) schedule (FI meaning "fixed interval"), the first completion of an FR10 sequence, with each completed sequence resulting in the brief presentation of a cocaine-associated light, at least 15 minutes after the previous cocaine infusion, would result in drug infusion. Clearly, incentive motivation must be very important in maintaining responding under these schedules, and the behavior is described as *drug seeking*.

Manipulations of the accumbens shell appear to be ineffective on second-order responding for cocaine. The results of manipulations of other brain regions previously implicated in cocaine reward, particular in regards to conditioned aspects, on responding with second-order schedules are somewhat surprising. Transient deactivation of the basolateral amygdala impaired acquisition of responding for cocaine under a second-order schedule, but it had little effect on previously acquired responding. Based on previously cited work, a large drop in acquired responding would be expected, due to the high degree of incentive motivation required for second-order performance. In addition, the blockade of glutamatergic transmission in the BLA by local injection of an AMPA antagonist also did not affect established responding. However, dopamine receptor blockade in the BLA by the broad-spectrum antagonist flupenthixol did reduce previously acquired responding.

Lesions of the accumbens core had little effect on lever-pressing for cocaine in which each press delivered the drug (FR1), but, like basolateral amygdala inactivation, reduced acquisition of second-order responding. Unlike in the BLA, transient inactivation of the accumbens core also decreased acquired responding on the second-order schedule. Injection of a glutamate antagonist for the AMPA receptor into the accumbens decreased responding for cocaine on a second-order schedule. Surprisingly, the blockade of dopamine receptors in the accumbens core with flupenthixol was ineffective on second-order responding for cocaine. However, this is consistent with a lack of

change in dopamine release in the accumbens core during second-order performance.

Broadly stated, the above pattern of effects is consistent with thinking that a glutamate releasing projection from the BLA to the core of the accumbens is important for second-order performance. The major problems with this scheme are the ineffectiveness of transient inactivation and glutamatergic blockade in the BLA on acquired responding. More recently, an experiment from the Everitt laboratory reported that unilateral dopamine blockade in the BLA, coupled with AMPA blockade in the accumbens core of the contralateral hemisphere, reduced acquired second-order responding for cocaine, supporting an amygdalo-accumbens projection system (Di Ciano & Everitt, 2004).

TRANSITION TO THE ADDICTED STATE

Descriptions of drug-addicted humans stress the compulsive nature of the activity. Obtaining the drug comes to dominate most other activities, even in the face of negative consequences. This final stage of addiction has only recently begun to receive attention from investigators using animal models. The major proposals in this area are reviewed below.

Everitt and colleagues, whose work on the role of drug-associated stimuli in maintaining drug taking has been previously surveyed, have proposed an anatomically oriented scheme for the addicted state (Everitt & Robbins, 2005). This concept relies on the knowledge, first developed nearly 40 years ago, of the role of the dorsal striatum in ritualized, stereotyped behaviors. The dorsal striatum consists of the caudate and putamen nuclei in primates, including humans. The two structures are present in the rat but fused into a single structure, often called the caudate-putamen, but nowadays simply called the dorsal striatum. This nomenclature distinguishes it from the ventral striatum, which includes the nucleus accumbens. Whereas the ventral striatum receives glutamatergic afferents—particularly from phylogenetically old "cortical" regions, including the hippocampus and basolateral amygdala (it has been argued the BLA is "cortical")—dorsal striatal glutamatergic afferents come heavily from neocortical regions. In fact, the entire neocortex maps topographically upon the dorsal striatum, with frontal regions projecting to the anterior dorsal striatum, sensorimotor cortex projecting to the midcentral dorsal striatum, and so on.

A burst of work, principally in the 1970s, revealed the importance of the dorsal striatum and of its dopaminergic afferents (which come from the substantia nigra rather than the VTA) in stereotyped behaviors induced by psychostimulants, notably amphetamine. High doses of amphetamine induce rats to repetitively lick and gnaw a limited area of the test chamber. Locomotor activity, which depends upon dopamine transmission in the accumbens, is largely absent as the animal engages in focused stereotypy. Stereotyped behaviors in nonhuman primates include behaviors such as repetitive picking at an area of skin. In humans, such behaviors can be more complex, such as repetitive housecleaning. Stereotyped behaviors are typically seen during IV self-administration of psychostimulants, particularly amphetamine, in rats. These may consist of the licking or gnawing of a particular spot, or there may be a distinct repetitive pattern of moving about in the chamber between lever-presses. Stereotyped behavior directed toward the lever can be lethal. Finally, stereotyped behaviors, like the locomotor behaviors induced by psychostimulants, show sensitization.

Destruction of the dopaminergic projection from substantia nigra to dorsal striatum attenuates or abolishes stereotypy in rats. Focal injection of amphetamine into the dorsal striatum, but not the nucleus accumbens, induces stereotypy in rats. At the neuroanatomical level, the involvement of the dorsal striatum in psychostimulant stereotypy is thought to reflect the inputs and outputs of the region. As previously mentioned, the inputs come particularly from neocortex. A major efferent projection of the nucleus accumbens is to the ventral pallidum, while a major output of the dorsal striatum is to the globus pallidus, which can be considered a "dorsal pallidum."

Everitt and Robbins have proposed that, in the development of addiction, control of drug-taking behaviors moves from the ventral striatum to the dorsal striatum. That is, drug-taking shifts from "instrumental action-outcome" control of behavior—in which the result of a response is compared to the expected result, thought to be mediated by the ventral striatal system—to "habit" control of behavior, thought to be mediated by the dorsal striatal system. Thus, when addiction is completely established, drug seeking and drug-taking are no longer based, as they were initially, on the reward of the drug, but on

stereotyped, compulsive behaviors. It is no surprise that current psychiatric work on obsessive-compulsive behavior has focused on systems linking the neocortex to the dorsal striatum, for the final state of addiction can be viewed as a variety of obsessive-compulsive behavior.

Supporting evidence from the laboratories of Everitt and Robbins includes findings that the release of dopamine by drug-paired stimuli does not occur in the nucleus accumbens of rats extensively trained on second-order schedules, but occurs instead in the dorsal striatum; and that dopamine receptor blockade in the dorsal striatum greatly reduces responding on a second-order schedule with cocaine, while (as previously mentioned) having no effect when the blockade is in the nucleus accumbens core.

The noted drug addiction researcher George Koob has proposed a different, although perhaps in the long run not incompatible, view of the "switch to addiction" (Koob & Le Moal, 2000; Koob & Kreek, 2007). When researchers first began using rodent models of drug self-administration, they found it technically difficult to keep the infusion line clear of blood clots and inhibit infection. Their way around these problems was to do the catheter implantation surgery, attach the animal to the infusion line in the test chamber, and let the animal live there for the duration of the experiment. The standard method is for the animal to live in its home cage and be brought to the test chamber for daily sessions lasting only one to two hours. Koob has argued that this method does not model the human addict, who moves from sporadic drug taking to a state where drug taking dominates existence. He suggests that the shorter access sessions model "recreational" drug use. By allowing rats to have much longer (6-hour) test sessions, he has found that the animals progressively increase their drug intake of both cocaine and opiates. This type of escalation does not happen with one-hour test sessions.

Koob and colleagues found that when the rats were infused with a single injection of cocaine, the locomotor response to the drug was diminished 14 days after an 8-day protocol of 6-hour access sessions for cocaine. If this was done after an 8-day protocol of 1-hour access sessions, a sensitized locomotor response was seen. Using these and other data, the Koob group has made the following argument: Sensitization may occur in the periodic "recreational" drug user. However, as the drug use progresses to a more chronic status, the response to the drug actually decreases, and any sensitization also decreases (Ben-Shahar et al., 2004). This is very similar to the more traditional idea of the development of tolerance in the chronic user. Koob and colleagues have shown that the threshold for rewarding brain stimulation (ICSS) of the hypothalamus progressively increases in the long-exposure rats when tested between drug-administration sessions. They believe this reflects a general *anhedonia* (loss of the appreciation of pleasure).

The scheme proposed by Koob and colleagues is similar, but much more advanced, than the traditional idea that a major, if not the major, reason the chronic user continues to take the drug is to stave off withdrawal. In a series of studies over a number of years, the Koob group has shown that during withdrawal from a number of drugs of abuse, the release of corticotropin-releasing hormone (CRH) within the brain in regions such as the amygdala is elevated. Intraventricular administration of CRH in rats evokes behaviors normally seen in conditions of fear and anxiety. (CRH antagonists reduce natural fear and anxiety in rats and are undergoing clinical trials as antidepressants in humans.) The Koob proposal is that, under long-access conditions, drug intake escalates, and this results in anhedonia for nondrug rewarding stimuli and depression or dysphoria. The rat (or human) continues to take the drug to stave off the dysphoric state, not because of the "pleasurable" effect of the drug itself.

SELF-CONTROL AND IMPULSIVITY

Work with human addicts has found increased levels of impulsive behavior in this population. It is not known, however, if the impulsivity predates the drug use or is a consequence of the drug use. In a publication by Belin and colleagues (2008), the Everitt and Robbins group has provided data supporting the idea that impulsive tendencies precede drug use. They screened rats for impulsivity using the five-choice serial reaction time task (5CSRTT). In this task, one of five apertures in a wall of the test chamber was illuminated for 0.5 seconds. The illuminated aperture varied, with a trial presented every 5 seconds. A nose-poke by the rat into the illuminated aperture resulted in a pellet delivery to a central food

magazine. Two kinds of errors are possible in this procedure: responses of commission (when a nose-poke is made in any aperture before illumination), and omission (when a nose-poke is not made into an illuminated aperture). After substantial training, accuracy is above 75 percent and omissions are below 20 percent. Data on impulsive responding (errors of commission) were collected during long 60-minute sessions. Other rats were screened for their locomotor response to a novel environment. On both the impulsivity and locomotor tests, rats scoring in the upper and lower quartiles were chosen for IV self-administration of cocaine.

These investigators separated acquisition of self-administration from addiction. Using previous studies, they defined addicted rats using a three-component criterion: (1) motivation to take the drug, (2) inability to refrain from drug seeking, and (3) maintained drug use despite negative consequences. Motivation to take the drug was determined by segmenting the self-administration sessions into three drug-access periods of 40 minutes separated by 15-minute drug-free intervals, and then counting responses during the drug-free intervals. The ability to refrain from drug seeking was determined by a progressive-ratio schedule breakpoint for responding. Intake despite negative consequences was determined by pitting drug intake again with electric footshock. Each rat received a total "addiction score" based on performance in each of the three components.

The results of Belin and colleagues (2008) clearly showed that while the locomotor response to novelty (HR/LR dimension)—in agreement with other work previously discussed—predicted rate of acquisition, it did not predict addiction as measured by the "addiction score." Conversely, premature responding in the impulsivity test did not predict acquisition but it did predict addiction. HR and high-impulsivity rats came from different populations and showed differences in distinct phases of the addictive process.

OVERVIEW OF RODENT RESEARCH ON DRUG ADDICTION

As listed at the beginning of this entry, work on understanding drug addiction using experimental animals suggests the following phases of the development of psychostimulant addiction:

1. Initial exposure to the drug gives a rewarding effect, which appears based on increased dopamine transmission, particularly in the shell of the nucleus accumbens. This is "recreational" drug use. Individuals show considerable differences in their response to the drug during this period: in some, the reward effect dominates; in others, an aversive anxiety effect curtails further drug use. Using the HR-LR (high-responder–low-responder) rat model, the difference between those in whom the reward effect dominates and those in whom the aversive anxiety effect dominates seems related to individual differences in response to stress in general. Although higher cortisol levels in response to stress are seen in HR individuals, their behavioral response is lower than that of LR individuals. The origin of the difference in stress reactivity, while of great interest, has no definitive answer at present. Genetic differences are likely, and environmental influences, particularly stress during early life, are thought to be important in setting the relevant neurobiological systems.
2. Continued exposure to the drug results in a sensitization of the rewarding effect. Again, this happens most readily in the HR-type individual. The sensitization appears to be based on plastic changes (changes in the brain that occur in response to experience) in synaptic transmission utilizing glutamate in the ventral tegmental area. The glutamate is thought to be released either from axons emanating from the prefrontal cortex or from axons of brainstem neurons driven by prefrontal neurons. In addition, the ventral tegmental-accumbens dopamine-using system, and the accumbens itself, appears very involved in incentive motivation for many kinds of rewarding stimuli. Thus, sensitization of incentive motivation, rather than the hedonic reward of the drug itself, has been proposed as the basis for continuing drug use.
3. Because of the initial hedonic reward effect and the subsequent incentive sensitization, drug use continues, resulting in an association of the drug state with external stimuli. These stimuli may be discrete (e.g., needle, sight of the drug) or contextual (e.g., a room). Discrete stimuli are thought to be linked to the nucleus accumbens–based motivational system (particularly the core subarea of the accumbens) via glutamate-using projections from basolateral amygdala. Contextual stimuli are thought

linked to this system via similar projections from the hippocampus. It is thought that the synaptic modifications in the systems are the same as those used elsewhere in the brain for the formation of long-term memories.

4. Relapse to drug use can be triggered by presentation of the drug, presentation of stimuli previously associated with the drug state, or stressful stimuli. The data from rat studies indicate that each of these relapse-inducing events, particularly stress, operate through somewhat unique brain areas and axonal connections.
5. With continued drug use, intake moves from being reward-based to being compulsive. It has been proposed that this entails a shift of the control of drug intake from the reward-based accumbens system to the habit-based dorsal striatum. Another view of the compulsive phase harks back to a more traditional view that physiological mechanisms have been altered by the drug, particularly by heavy drug use, resulting in a new state from which deviation is aversive. These two views are not mutually exclusive.
6. Finally, very recent work with rats suggests that the propensity to traverse all the above stages leading up to addiction only happens in approximately 20 percent of the animals tested, and that it can be predicted by pre-exposure behavioral impulsivity.

Viewed through a historical lens, it is interesting to note that the view of drug addiction, after all the neurobiological work, seems to be returning to the human-based view of decades ago. That is, some are returning to the view that addiction is a kind of compulsion, that aversion to withdrawal plays a major part in maintaining it, and that self-control ("impulsivity") is important in developing and maintaining it.

See also **Addiction: Concepts and Definitions; Antagonist; Brain Structures and Drugs; Conditioned Tolerance; Craving; Dopamine; Dose-Response Relationship; Glutamate; Reinforcement; Relapse; Research: Aims, Description, and Goals; Research: Clinical Research; Research: Measuring Effects of Drugs on Behavior; Reward Pathways and Drugs; Tolerance and Physical Dependence.**

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DARRYL NEILL

REWARD PATHWAYS AND DRUGS.

Two sources of reinforcement can be found in drug-taking behavior associated with the use, abuse, and addiction to drugs: positive and negative reinforcement. Positive reinforcement occurs when presentation of a drug increases the probability of a response to obtain the drug. Animal models of the positive reinforcing or rewarding effects of drugs are extensive and well validated. They include intravenous drug self-administration, conditioned place preference, and brain stimulation reward. Drugs of abuse are readily self-administered by animals that are not dependent; therefore, positive reinforcement and intravenous drug self-administration have been used to predict abuse liability.

Negative reinforcement occurs when presentation of the drug prevents the aversive consequences of removal of the drug, usually in the context of drug dependence. Animal models of the negative reinforcement associated with drug dependence include measures of conditioned place aversion (rather than preference) to precipitated withdrawal or spontaneous withdrawal from chronic administration of a drug, increases in reward thresholds using brain stimulation reward, and dependence-induced increases in drug-taking and drug-seeking behavior. Such increased self-administration in dependent animals has been observed with cocaine, methamphetamine, nicotine, heroin, and alcohol.

BRAIN REWARD PATHWAYS

Electrical brain stimulation reward (or intracranial self-stimulation) has a long history as a measure of activity of the brain reward system and of the acute reinforcing effects of drugs of abuse. Brain stimulation reward involves widespread neurocircuitry in the brain, but the most sensitive sites defined by the lowest thresholds involve the trajectory of the medial forebrain bundle connecting the ventral tegmental area with the basal forebrain (Olds & Milner, 1954). While much emphasis was focused initially on the role of the ascending monoamine systems in the medial forebrain bundle, other non-dopaminergic systems in the medial forebrain bundle clearly have a key role (Hernandez et al., 2006).

EFFECTS OF DRUGS OF ABUSE ON BRAIN REWARD THRESHOLDS

All drugs of abuse, when administered acutely to nondependent animals, decrease brain stimulation reward thresholds (Kornetsky & Esposito, 1979). Measures of brain reward function during acute abstinence from all major drugs with dependence potential have revealed increases in brain reward thresholds measured by direct brain stimulation reward. These increases in reward thresholds may reflect decreases in the activity of reward neurotransmitter systems in the midbrain and forebrain implicated in the positive reinforcing effects of drugs (Koob et al., 2004).

NEUROCIRCUITRY OF POSITIVE REINFORCEMENT ASSOCIATED WITH DRUGS OF ABUSE

The acute reinforcing effects of drugs of abuse are mediated by the activation of dopamine, serotonin, opioid peptides, and gamma-aminobutyric acid (GABA) systems, either by direct actions in the basal forebrain (notably the nucleus accumbens and central nucleus of the amygdala) or by indirect actions in the ventral tegmental area (Koob & Le Moal, 2001). Much evidence exists to support the hypothesis that the mesolimbic dopamine system is dramatically activated by psychostimulant drugs during limited-access self-administration and to some extent by all drugs of abuse. Serotonin systems, particularly those involving serotonin 5-HT_{1B} receptor activation in the nucleus accumbens, also have been implicated in the acute reinforcing effects of psychostimulant drugs. Opioid peptides in the ventral striatum have been hypothesized to mediate the acute reinforcing effects of ethanol self-administration, largely based on the effects of opioid antagonists. Mu opioid receptors in both the nucleus accumbens and ventral tegmental area mediate the reinforcing effects of opioid drugs. GABAergic systems are activated pre- and postsynaptically in the amygdala by ethanol at intoxicating doses, and GABA antagonists block ethanol self-administration (Koob, 2006; Nestler, 2005).

NEUROCIRCUITRY OF NEGATIVE REINFORCEMENT ASSOCIATED WITH DRUGS OF ABUSE

During the development of dependence, the brain systems in the ventral striatum that are important for the acute reinforcing effects of drugs of abuse, such as dopamine and opioid peptides, become compromised and begin to contribute to a negative reinforcement mechanism. Here, the drug is taken to restore the decreased function of the reward systems. However, the extended amygdala, a neuroanatomical entity with neurotransmitter systems that have been implicated in stress, is involved in the negative reinforcement associated with drug taking during dependence. The extended amygdala is composed of the central nucleus of the amygdala, the bed nucleus of the stria terminalis, and a transition zone in the medial (shell) subregion of the nucleus accumbens (Heimer & Alheid, 1991). Several key neurotransmitters localized to the extended amygdala, such as corticotropin-releasing factor (CRF), norepinephrine, and dynorphin, have been shown to be activated during stress, in anxiety-like states, and during drug withdrawal in dependent animals. More importantly, antagonists of these neurochemical systems selectively block drug self-administration in dependent animals, suggesting a key role for these neurotransmitters in the extended amygdala in the negative reinforcement associated with drug dependence.

ROLE OF POSITIVE AND NEGATIVE REINFORCEMENT MECHANISMS IN ADDICTION

The brain reward system is thus implicated in both the positive reinforcement produced by drugs of abuse (ventral striatum) and the negative reinforcement produced by dependence (extended amygdala). Neuropharmacological studies in animal models of addiction have provided evidence for the dysregulation of specific neurochemical systems (dopamine, opioid peptides, GABA) in the ventral striatum associated with positive reinforcement (reward). Recruitment of brain stress systems (CRF, dynorphin, and norepinephrine) in the extended amygdala provides the negative motivational state associated with drug abstinence. The changes in reward and stress systems are hypothesized to contribute to the increased motivation to take drugs in dependence and to remain outside a homeostatic state post-acute dependence, and as such they contribute to the vulnerability for relapse in addiction.

See also **Research, Animal Model: An Overview.**

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GEORGE F. KOOB

RHETORIC OF ADDICTION.

Typically drug and alcohol researchers answer the question, "What is addiction?" by identifying a biological or psychological process that takes place within an individual and then determining whether this process is best understood as a disease, a disorder, a syndrome, or a learned behavior. This approach implies that there is a universal truth of addiction underlying the observed diversity of addictive symptoms and experiences. Scientific research is seen as the key to revealing the truth of addiction; in particular, neurological models of reward have become prominent in

explaining the ability of alcohol and drugs to produce dependence (Koob et al., 1990).

However, there is a very different approach to understanding addiction that shifts the discussion from the question of what addiction really is. Instead, it focuses on addiction as a particular way of thinking and talking about problems of desire, consumption, and self-control. This rhetorical or discursive approach emphasizes the role of language in shaping beliefs and experiences. It is influenced by the work of post-structuralist philosopher Michel Foucault (1926–1984), who argued that discourses systematically produce the objects and subjects of which they speak. Moreover, discourses determine what can be said about a topic and what can be recognized as true (Foucault, 1971).

The discursive approach examines, therefore, how different institutions and forms of knowledge, including medicine, law, government, education, self-help literature, twelve-step groups, and popular culture construct addiction. While the notion of addiction as a discrete disease or disease-like entity has become dominant, different discourses produce different understandings of addiction, and contradictions and tensions also exist within discourses (Reinarman, 2005). Thus, the identity of addiction and the identity of the addict are mobile and elusive. Depending on the discursive context, the addict may be a sinner requiring redemption, a patient requiring treatment, a tragic victim requiring help, a criminal requiring punishment, or an educator with a unique insight into the dangers of alcohol and drugs.

The proliferation of addictions that took place during the 1980s and 1990s heightened the impact of discursive analyses. As addiction discourse expanded to include objects and activities such as food, sex, work, and exercise, its expression of specific cultural and moral anxieties became increasingly visible. For example, sex addiction emerged at a time when the HIV/AIDS epidemic resonated with the idea of lust and sex as dangerous and uncontrollable forces (Irvine, 1995). More broadly, as literary theorist Eve Sedgwick has argued, addiction discourse is driven by a hierarchical dichotomy in which rationality and freedom of will are constantly threatened by compulsive desire. The more people subject their desires to scrutiny, looking for the perfect space of freedom, the more elusive this freedom becomes as every desire is revealed to be compromised by compulsion (Sedgwick, 1995).

The expansion of addiction also revealed tensions in medical models. On the one hand, medical discourse stressed the importance of distinguishing between genuine substance addictions and popular notions such as food addiction (Miller, 1995). On the other hand, the emphasis on the subjective experience of compulsion and the presence of harmful consequences in diagnosing addiction, found in the *DSM-IV* criteria for substance dependence, suggests that the disorder can be produced by objects and activities other than psychoactive drugs (American Psychiatric Association, 1994).

One effect of taking a discursive approach to addiction is that the historical and cultural specificity of the concept is highlighted. Rather than being a universal feature of human existence, addiction is a specific way of classifying and regulating certain problems of individual conduct. In his 1978 article "The Discovery of Addiction," Harry Levine describes the pre-modern world as a world without addiction. He argues that while heavy drinking and habitual drunkenness certainly existed in colonial America, this behavior was not viewed as pathological. The notion of alcoholism as a disease of the will only developed in the nineteenth century with the rise of the temperance movement and its vision of the desire for drink as a force that could take over the drinker's life. Social and economic changes that made self-control and discipline crucial traits for success also occurred at this time, enhancing the impact of the addiction concept. Loss of control continues in the twenty-first century to be a central feature of both popular and medical accounts of addiction. As many critics have observed, the threat of losing self-control acquires resonance in individualistic societies in which a person's internal qualities are taken to be the determinants of success and happiness (Room, 2003). Indeed the disorder of addiction makes sense because of a belief in the possibility and importance of self control along with recognition of its fragility.

AA DISCOURSE

Alcoholics Anonymous and other self-help recovery groups have produced an influential and distinctive addiction discourse built around the notion of alcoholism and other addictions as incurable diseases of the self. While the disease entity described in self-help

literature is dismissed by some medical experts as vague and unsupported by evidence, its linking of physical and spiritual malaise clearly captures the experience of addiction for many (Keane, 2002). In AA discourse, alcoholism is a biomedical disease with specific symptoms and a predictable course. But more importantly, it is also a moral sickness characterized by self-pity, self-centeredness, and dishonesty; hence recovery requires personal transformation as well as abstinence from alcohol. This hybrid model of disease is central to AA's pragmatic yet demanding approach to recovery. In the *12 Steps of Alcoholics Anonymous*, the inner self is constructed as an object for inspection and rectification. A habit of vigilant self-monitoring is the price of recovery, but lapses are accepted as part of the process (Nowinski & Baker, 1998).

A central feature of AA discourse is the construction of addiction as an identity, rather than a behavior. According to AA, an alcoholic is fundamentally different from a normal drinker, and an alcoholic with twenty years of sobriety is still an alcoholic. To critics, envisioning addiction as an all-encompassing and inescapable master identity that explains everything about a person is restrictive, makes the person pathological, and is not mindful enough of the social factors that encourage harmful forms of consumption (Keane, 2002). But for other commentators, the sense of identity encapsulated in the ritual statement, "I am James and I am an alcoholic," is a powerful expression of community membership and personal transformation. In his sympathetic account of AA discourse, George Jensen argues that this phrase combines both a before and after self; a past self who drank and a present self who does not drink and is trying to live in a new way (2000). The same discourse is open to multiple interpretations, but the autobiographical and confessional mode of self-presentation encouraged by AA is unmistakable (Alasuutari, 1992).

MEDICAL DISCOURSE

In contrast, medical and scientific discourse on addiction presents itself as objective and rational, an antidote to the moral judgment and sensationalism found in popular and public arenas. Neurological accounts of addiction that highlight the effect of drugs on brain chemistry have the authority of a hard science supposedly uncontaminated by cultural and social factors. Their success has depended in part on advances in brain imaging technologies. Research that uses positron emission tomography (PET) and magnetic resonance imaging (MRI) scans to demonstrate the difference between the addicted and non-addicted brains is rhetorically powerful because these images are seen as revealing the so-called hidden reality of the brain. But these computer-generated images do not provide unmediated access to a hidden object; rather, they translate non-visible phenomena into visual representations. When a cocaine-using subject's neurotransmitter activity is translated into a pattern of color and contrasted with the pattern produced by a brain categorized as normal, a particular conception of addiction as a discrete disorder located within in an individual is made concrete (see Grant et al., 1996). Such images are part of a discourse of addiction, not objective external proof of the validity of that discourse. Their meaning relies on a prior classification of individuals into addicted/not addicted and unhealthy/healthy that is based on an assessment of behavior rather than biological or chemical markers.

The process of diagnosing addiction further demonstrates the limits of objectivity in medical discourse as it relies on judgments about what a so-called normal life looks like, how an apparently healthy body functions, and how personal priorities should be organized. Diagnostic guidelines and screening tests for alcoholism emphasize the subject's feelings and thoughts rather than specifying a level of consumption or physical markers of excessive intake (Valverde, 1998). Is the drinker preoccupied with drinking? Does the drinker feel compelled to drink? Does the drinker feel guilty or worried about habitual drinking? Withdrawal and tolerance are listed in the *DSM-IV* criteria but are not necessary for a diagnosis of substance dependence. What is being identified is not a biological state so much as a pathological relationship to the substance, in which drinking or drug use has assumed too high a priority.

Moreover, the existence of compulsion or impaired control, which is central to the diagnosis of addiction, can only be ascertained through self-reported experiences or behavior observed by others. Binge drinking, staying drunk for days at a time, drinking more than one intended to when one began, and neglecting responsibilities because of drinking are frequently read as signs of compulsion. But the meaning of these experiences is profoundly influenced by social and cultural

context, and thus they seem less than robust as the basis for the identification of a disease or disorder (Measham & Brain, 2005). For example, the utility of *neglect of responsibilities* as a measurement of loss of control depends on the salience of those responsibilities to the individual.

A related feature of addiction that is stressed in medical models is continued drug and alcohol use despite harmful consequences such as job loss, relationship conflicts, and health problems. This feature takes for granted a certain level and style of social functioning, assuming that in the absence of drug use, the individual would not be facing issues such as unemployment and poverty. It also assumes middle-class norms of respectability: For a sex worker or bartender, heavy drinking could aid rather than hinder job performance (Valverde, 1998). Drug use can also facilitate as well as impede relationships and time management; for some, it is quitting that brings loneliness and lack of structure. The interpretation of social harms as signs of addiction can lead to a circular logic in which the existence of work and family problems defines addiction and addiction implies the presence of work and family problems. This process can result in the almost automatic attribution of pathology to members of negatively valued groups such as welfare mothers or unemployed youth (Keane, 2005).

DISCOURSE, POWER AND EXPERIENCE

Discursive analyses draw attention to the exercise of power in descriptions and attributions of addiction. Addiction discourses promote the expansion of expert and governmental power over individuals, and while they may have beneficial as well as oppressive effects, their combination of medical and ethical judgment gives them a potent ability to categorize and regulate. Moreover, their classification of bodies and subjects often coincides with existing hierarchies of social value, reproducing inequalities of race, class, sex, and sexuality. For example, while claiming an addict identity may be a useful strategy for a rich white celebrity caught using drugs, poor black mothers identified as addicted are liable to face demonization and punitive intervention (Campbell, 2000). More generally, while conceptualizing addiction as a disease can undermine moralistic accounts of addicts as simply weak-willed, addicts are placed in an infantilized position in which their own views about their predicament can be dismissed if they contradict expert opinion (Sedgwick, 2005).

Discourse analysis has been criticized for privileging texts, language, and theory at the cost of engaging with the lived and embodied reality of individual experience (Ramazanoglu, 2002). In the case of addiction, the danger of minimizing the terrible impact of compulsive behaviors on many people's lives and the magnitude of their struggles to change their behavior are seen as especially acute. It is the case that discursive scholarship destabilizes the notion of experience by focusing on the way experience is constructed, and it is undeniable that therapeutic outcomes are not its primary concern. However, in critically examining the authoritative and complex forms of knowledge that frame individual experiences of addiction and the range of possible responses to that experience, studies of discourse and rhetoric are an essential component of addiction research.

See also **Addiction: Concepts and Definitions.**

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HELEN KEANE

RISK FACTORS FOR SUBSTANCE USE, ABUSE, AND DEPENDENCE

This entry includes the following essays:

AN OVERVIEW

Risk factors for use, abuse, and dependence on alcohol and drugs are characteristics of individuals or environments that increase risk. Such factors are not absolute determinants of alcohol and drug use or problems but, rather, factors that affect the probability that individuals with these factors will use, abuse, or become dependent on a given substance.

Much individual variation occurs within groups and societies in alcohol and drug use, abuse, and dependence. Some people never use substances although they are readily available in their environments. Others use drugs sporadically or regularly for a short time, or for years, and yet never become dependent. Others become dependent but remit, whereas still others become chronic heavy users who cannot stop despite great costs to themselves and those close to them. The various patterns of use result from a complex combination of environmental and genetic factors.

Risk factors for substance use, abuse, and dependence have been reported at various levels ranging from macro or large-scale societal factors to the molecular level. Large-scale changes in the prevalence of use over time in society indicate shifting macro-level factors. For alcohol, good sources of information on long-term time trends in the U.S. are per capita alcohol consumption statistics (http://pubs.niaaa.nih.gov/). For drugs, a good source of information on time-term time trends is the information from yearly surveys of U.S. high school and college students known as Monitoring the Future (http://www.monitoringthefuture.org). General articles about sociodemographic risk factors for alcohol abuse and dependence (Hasin et al., 2007a; Compton et al., 2007) in 2001 and 2002 in the United States show that among adult residents of households or group quarters (such as college dormitories), a current or lifetime history of alcohol or drug abuse or dependence was associated with being male, younger, unmarried, of lower socio-economic status, and being white or Native American compared to black, Hispanic, or Asian race/ethnicity.

Macro-level factors affecting use of alcohol and drugs include influences such as laws (local or nationwide) against any use or sales (e.g., drugs) or laws that target certain age groups (e.g., minimum drinking age laws) (Voas et al., 2003; Hingson et al., 1998). An example is the Eighteenth Amendment to the U.S. Constitution, which from 1920 to 1933 outlawed the manufacture, transport, and sale of alcohol. This law was effective in limiting alcohol consumption in the United States. Some scholars

believe its unpopularity led to its demise, while others maintain that the amendment was repealed because it was not enforceable and may have actually caused crime to escalate. The strength of law enforcement has also been shown to influence use. Pricing is another macro-level factor that affects alcohol and drug use, as higher prices tend to decrease use (Chaloupka et al., 2002). Availability influences use; for example, the density of alcohol outlets within given geographic areas can affect the proportion of substance users. (LaScala et al., 2001). Advertising and marketing strategies can also influence the use of legal substances, for example, alcohol and cigarettes.

In terms of more local environmental influences, adolescent peer groups have long been shown to influence substance use (Walden et al., 2004; Agrawal et al., 2007). However, while peer groups may provide modeling of substance use and access to substances, recognition has increased that adolescents with certain partially heritable personality traits may seek peer groups that include substance abusers (Kendler et al., 2007). Consequently, the relationship between substance-using peer groups and adolescent substance use is not entirely causal.

External traumatic or stressful experiences can increase the use of substances, as has been shown by both animal and human studies. Childhood abuse is a risk factor for use of substances and for becoming dependent on them (Nelson et al., 2006; Kendler et al., 2000). The role of adult stressors is more difficult to determine because some personality traits associated with substance use (e.g., sensation seeking) may also increase the risk for traumatic experiences such as serious accidents. In such cases, an apparent relationship between accidents and subsequent substance use could actually be due to the common underlying sensation seeking personality trait, and attributing the substance use to the accident would be incorrect. A study that overcomes this difficulty is one that examines adolescent or adult civilian exposure to terrorism, since such exposure to traumatic experiences is independent of any personality or other personal characteristics and thus serves as a type of so-called natural experiment for understanding the relationship of stress exposure and subsequent alcohol or substance use. A series of studies in the United States and Israel have shown that adolescents' exposure to terrorism increases the risk for use of alcohol and drugs (Schiff et al., 2007; Wu et al., 2006) and adults (Hasin et al., 2007b).

While no single personality trait predicts alcoholism (Sher et al., 2005), traits associated with the development of substance use disorders include novelty seeking (Cloninger et al., 1995) and sensation seeking (Zuckerman & Kuhlman, 2000; Martin et al, 2004). These traits also have their own risk factors, which include environmental and genetic influences.

Cognitive factors that affect the risk for substance use and substance use disorders include expectancies and motivations. *Expectancies* (positive or negative) are beliefs about the expected effects of alcohol or another substance, that is, that use will make the user more social, feel good, or lead to some sort of problem (Goldman & Rather, 1993). A twin study indicated that alcohol expectancies are due to environmental rather than genetic influences (Slutske et al., 2002). Motivations are the reasons that individuals actually use the substances, that is, to socialize, to fit in, because the effects are enjoyable (Cooper et al., 1995). Drinking to cope with negative feelings and emotions has been associated with problem drinking in a number of studies (Mann et al., 1987; Carpenter & Hasin, 1998; Beseler et al., 2008). While expectancies and motives are related, they are not necessarily entirely overlapping.

Neuroscientists investigate aspects of brain functioning and neurotransmission as risk factors or causes of alcohol and drug use, abuse, and dependence. In addition, genetic influences are known to affect the risk for alcohol and drug use and dependence.

See also **Abuse Liability of Therapeutic Drugs: Testing in Animals; Addiction: Concepts and Definitions; Complications: Mental Disorders; Conduct Disorder and Drug Use; Epidemiology of Drug Abuse; Models of Alcoholism and Drug Abuse.**

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DEBORAH HASIN

DRUG EFFECTS AND BIOLOGICAL RESPONSES

Although many indirect factors lead to an individual abusing drugs, a person's response to the effects of the drugs themselves contribute both to their use and abuse. These drug effects should be considered in relation to four phases of drug use: (1) initiation-consolidation, (2) maintenance, (3) repeated withdrawal and relapse, and (4) postwithdrawal. During the initiation-consolidation phase, behaviors that lead to the taking of a drug are gradually strengthened through operant and classical conditioning processes and by biochemical changes in the brain. The drug effects include a cascade of discriminative or internally appreciated drug cues (i.e., subjective effects). The presence of these cues often leads to associated autonomic responses and reports of urges in humans. These responses and urges may result in an unfolding of a sequence of behavioral and physiological events leading to continued drug consumption.

After a pattern of chronic drug use is established, individuals may become tolerant to certain effects of a drug. In addition, they may experience withdrawal effects when they stop taking a drug. Withdrawal effects are often opposite to the drug-induced state and usually involve some form of dysphoria—a state of illness and distress. Over time, withdrawal effects become associated with stimuli in the environment, as was the case for the euphoric and other direct effects of the drug. Because of operant and classical conditioning processes, these associated stimuli can then produce conditioned effects that are often characterized as urges or cravings, and that may trigger relapse.

The underlying neurotransmitter systems within the brain, subserving these behavioral features of drug effects, are just beginning to be understood. Early research on the neural substrates of reward in general used electrical brain stimulation as the reward. For example, Olds (1977) found that rats would press a lever to receive a brief electrical pulse to the hypothalamus; rats would press this lever to such an extent that they did not engage in consummatory reward activities such as eating and drinking. Subsequent research indicated that activation of certain systems in the brain, namely the mesolimbic and nigrostriatal dopaminergic systems, were most sensitive to brain stimulation reinforcement. Several theories have been suggested to explain the importance of the brain reward system for the survival of species (Conrad, 1950; Glickman & Schiff, 1967; O'Donahue & Hagmen, 1967; Roberts & Carey, 1965).

Further research demonstrated that most drugs of abuse lower the threshold for this brain stimulation reward, thus suggesting that such drugs may activate the same, or similar, reward pathways (see Koob & Bloom, 1988). As will be seen, furthermore, the reinforcing effects of the drugs themselves—that is, effects that lead individuals to take the drugs—are directly mediated by these reward systems. The fact that many drugs induce activation of these systems may indicate a mechanism underlying the addiction-related effects of drugs of abuse.

COCAINE AND OTHER STIMULANTS

Cocaine is an indirect catecholamine agonist that acts by blocking the reuptake of monoamines, including dopamine (DA), norepinephrine (NE), and serotonin (5-HT). During the process of reuptake, the previously released neurotransmitter is actively transported back from the synaptic cleft into the presynaptic terminal of the neuron where the neurotransmitter was produced and released (Pitts & Marwah, 1987). In contrast to cocaine, amphetamine acts not only by inhibiting uptake, but also by releasing catecholamines from newly synthesized storage pools from the presynaptic terminal of the neuron (e.g., Carlsson & Waldeck, 1966).

Amphetamine and cocaine are both potent psychomotor stimulants. They produce increased alertness and energy and lower anxiety and social inhibitions. The acute reinforcing actions of the stimulants are primarily determined by their augmentation of DA systems. With prolonged consumption: (1) acute tolerance becomes substantial, and (2) the individual starts to regularly consume higher and many more doses if the resources are available. Over time, in high-dose regimens, the behavioral pattern of use becomes stereotyped and restricted. In settings of low availability, the individual focuses on the acquisition and consumption of the drug. These effects of stimulants occur within weeks or months of continued use. The individual may also start "bingeing" during this period. A binge is characterized by the readministration of the drug approximately every ten

to twenty minutes, resulting in frequent mood swings (i.e., alternations of highs and lows). Cocaine binges typically last twelve hours, but may last as long as seven days.

It has been proposed that cocaine abstinence consists of a three-phase pattern: crash, withdrawal, and extinction (Gawin & Kleber, 1986; Gawin & Ellinwood, 1988). The crash phase immediately follows the cessation of a binge and is characterized by initial depression, agitation, and anxiety. Over the first few hours, drug craving is replaced by an intense desire for sleep. During this time, the individual may use alcohol, benzodiazepines, or opiates to induce sleep. Following the crash, hypersomnolence (excessive sleep) and hyperphagia (excessive appetite) develop. Following the first few days of hypersomnolence and hyperphagia, other symptoms emerge that are the opposite of the effects of cocaine—withdrawal symptoms. During this withdrawal period, which lasts three to ten days, individuals experience decreased energy, limited interest in their environment, and anhedonia. They are also strongly susceptible to relapse and starting another binge cycle (Gawin & Ellinwood, 1988; Gawin & Kleber, 1986). This phase is followed in time by the extinction phase, in which relapse to cocaine use is prevented. During the extinction phase, brief periods of drug craving also occur. These episodes of craving are thought to be triggered by conditioned stimuli that were previously associated with the drug. If the individual experiences these cues without the associated drug effects—that is, resists relapse—then the ability of these cues to elicit drug cravings should diminish over time, which in turn should lessen the probability of relapse (Gawin & Ellinwood, 1988).

As already noted, acute administration of cocaine produces profound inhibition of dopaminergic uptake (Fuxe, Hamberger, & Malmfors, 1967). The relation between cocaine dose and DA levels is linear; therefore, larger amounts of cocaine result in higher extracellular DA levels. These levels of DA are thought to underlie the reinforcing effects of cocaine (Gawin & Ellinwood, 1988). Because both cocaine and amphetamine result in enhanced dopaminergic neurotransmission, thereby producing elevated extracellular levels of catecholamines, these elevated neurotransmitter levels would presumably have local time-dependent inhibitory effects on the enzyme tyrosine hydroxylase, which is responsible for controlling their rate of synthesis. Therefore, this substrate-inhibitory mechanism might compensate for the increased catecholamine levels and activity by decreasing their synthesis. Galloway (1990) found that cocaine, in a way that was consistent with this proposition, decreased DA synthesis in a dose-dependent manner in various brain regions.

	Amphetamine		Cocaine	
	Day I	Day 7	Day 1	Day 7
Autoreceptor sensitivity	sub	super	sub	super
Receptors	decreased	decreased	unclear	unchanged
Biosynthesis	reduced	reduced	unchanged	unchanged
Uptake sites	decreased	decreased	unchanged	unchanged

Table 1. Effects of chronic cocaine and amphetamine administration on dopaminergic functioning. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Chronic, intermittent stimulant use (e.g., 1–2 injections per 24 hrs) produces other behavioral effects besides euphoria and increased energy: (1) stimulant psychosis, which is characterized by paranoia, anxiety, stereotyped compulsive behaviors, and hallucinations, and (2) sensitization or "reverse tolerance." Sensitization refers to the fact that the effects of cocaine are progressively enhanced. Although sensitization has been demonstrated in animal studies, it is not clear whether it occurs in humans. There are nevertheless several possible explanations for sensitization. First, because cocaine blocks dopaminergic uptake, chronic cocaine use could somehow harm the functioning of the dopamine uptake mechanism; the evidence regarding this possibility is equivocal (Zahniser et al., 1988b). Second, sensitization could also be the result of enhanced dopaminergic release, similar to that found to be chronic after amphetamine administration (Castaneda, Becker, & Robinson, 1988). Akimoto, Hammamura, & Otsuki (1989) found enhanced DA release in the striatum one week following chronic cocaine administration. Similar data has been obtained by others (Kalivas et al., 1988; King et al., 1993a; Pettit et al., 1990). Cocaine levels in blood and cerebrospinal fluid have also been reported to be elevated in chronically treated subjects (Reith, Benuck, & Lajtha, 1987); however, these

increases cannot account for most of the change in DA release (Pettit et al., 1990). Furthermore, some researchers report no consistent effects in this regard. Third, there could be changes in autoreceptor sensitivity following chronic cocaine administration. Autoreceptors for particular neurotransmitters are those receptors that reside on the same neuron that releases the neurotransmitter. The autoreceptors on the somatodendritic area of neurons regulate impulse flow along the neuron, whereas autoreceptors on the terminal regions of the neuron regulate the amount of neurotransmitter released per impulse and neurotransmitter synthesis (Cooper, Bloom, & Roth, 1986). Sensitization could, therefore, be the result of decreased autoreceptor sensitivity. Such subsensitivity would result in either increased impulse flow, if somatodendritic autoreceptors were altered, or increased neurotransmission/synthesis, if terminal autoreceptors were altered. The net effect, in either case, would be an increase in dopaminergic neurotransmission. There is some evidence of decreased somatodendritic autoreceptor sensitivity 24 hours after the cessation of chronic cocaine administration (Henry, Greene, & White, 1989). However, seven days after termination of daily cocaine injections, when cocaine-induced sensitization is still fully present, somatodendritic autoreceptors are no longer reduced in sensitivity (Zhang, Lee, & Ellinwood, 1992). Evidence regarding changes in terminal autoreceptor sensitivity is mixed. Dwoskin and colleagues (1988) found that terminal autoreceptors were supersensitive, not subsensitive, to a DA agonist 24 hours following chronic cocaine use. Henry and associates (1989) also found that terminal autoreceptors were supersensitive to DA following chronic daily cocaine injections. Although autoreceptor supersensitivity cannot explain sensitization, it is a possible mechanism underlying the previously described anhedonia and anergy experienced by cocaine abusers during the withdrawal phase. Fourth and last, there could be an increase in the number or sensitivity of postsynaptic DA receptors. The evidence regarding this hypothesis is also mixed (Zahniser et al., 1988a). For example, Peris and colleagues (1990) found an increased number of postsynaptic D2 receptors in the nucleus accumbens one day following cessation of chronic cocaine administration; however, after one week the number of receptors had returned to normal levels. In contrast, there is some evidence that postsynaptic DA receptors are decreased following chronic cocaine use. Volkow et al. (1990) found lower uptake values for [18 F]n-methylspiroperidol in human cocaine users who had been abstinent for one week, as compared with normal subjects. Uptake values were similar, however, for normal subjects and cocaine users who had been abstinent for one month.

In contrast with these results, Yi and Johnson (1990) have reported that chronic intermittent cocaine use impairs the regulation of synaptosomal 3[H]-DA release by DA autoreceptors, thus suggesting a subsensitivity or down-regulation of release-modulating DA autoreceptors seven days after chronic cocaine administration. The differences in the results of the Yi and Johnson (1990) and the Dwoskin et al. (1988) studies may be due to differences in the administration schedules or in the procedures used to measure autoreceptor sensitivity.

In contrast with the changes induced by intermittent but chronic drug administration, a regimen that involves the chronic administration of steady-state levels of drug results in decreased DA overflow when striatal brain slices are perfused with cocaine. This result may be due to the development of supersensitive autoreceptors. Autoreceptor supersensitivity would result in decreased dopaminergic activity. There is some support for this hypothesis from research involving the chronic administration of amphetamine. Lee and colleagues (Lee, Ellinwood, & Nishita, 1988; Lee & Ellinwood, 1989) found that 24 hours after withdrawal from a week of continuous administration of amphetamine, all indicators of autoreceptor activity demonstrated a pronounced subsensitivity. Similar results have been found following the continuous infusion of cocaine (Zhang et al., 1992). However, by the seventh day of withdrawal (a period associated with anergia, irritability, and "urges" in human stimulant abusers), nigrostriatal somatodendritic autoreceptors progress from an initial subsensitivity to a supersensitive state, whereas terminal autoreceptors are normosensitive. The changes in sensitivity of receptors clearly depend on the way the drug is administered and which receptors are evaluated. The evidence, moreover, is not always consistent.

There is also evidence that chronic cocaine administration produces neurotoxicity—i.e., actual destruction of neural tissue—although there are conflicting results and the relationship of this neurotoxicity to the addiction process is unclear. For example, Trulson and colleagues (1986) demonstrated decreased tyrosine hydroxylase activity sixty days after chronic cocaine treatment (see also Trulson & Ulissey, 1987), thereby indicating decreased DA synthesis. (Tyrosine hydroxylase is the rate-limiting step in the biosynthesis of DA; Cooper et al., 1986.) Similarly, Taylor and Ho (1978) found that chronic administration of cocaine decreased tyrosine hydroxylase activity in the caudate, but Seiden and Kleven (1988) were unable to replicate the findings of Trulson. As contrasted with the inconclusive results on cocaine, research involving amphetamine is much clearer. First, chronic methamphetamine administration reduces the number of DA uptake sites (Ricaurte, Schuster, & Seiden, 1980; Ricaurte, Seiden, & Schuster, 1984). Second, DA and tyrosine-betahydroxylase levels are reduced for extended periods following chronic amphetamine administration (Ricaurte et al., 1980, 1984). Third, there is evidence of neuronal degeneration, chromatolysis, and decreased catecholamine histofluorescence (Duarte-Escalante & Ellinwood, 1970).

As with cocaine's effects on DA reuptake, cocaine also blocks 5-HT reuptake. Since activation of 5-HT postsynaptic receptors affects neurotransmission in neurons that release DA, this blockade prolongs the inhibitory effects of 5-HT on dopaminergic neurotransmission (Taylor & Ho, 1978). However, cocaine also inhibits the firing rates of dorsal raphe 5-HT neurons (Cunningham & Lakoski, 1988, 1990). Thus, acutely the net effect of cocaine on 5-HT neurotransmission in the nucleus accumbens will depend on the relative contributions of uptake inhibition, which would increase synaptic 5-HT, and inhibition of neuronal firing, which would decrease synaptic 5-HT. Broderick (1991) reported that acute, subcutaneous injections of cocaine resulted in a dose-dependent increase in DA levels, as measured by dialysis of the nucleus accumbens. This suggests a decrease in 5-HT levels that may result from activation of somatodendritic 5-HT autoreceptors located in the dorsal raphe nucleus. Acute cocaine administration has indeed been reported to almost completely inhibit the basal firing rate of dorsal raphe serotonergic neurons.

As with the effects of chronic amphetamine administration on the functioning of DA systems, chronic methamphetamine administration has been shown to induce pronounced long-term changes in tryptophan hydroxylase activity, as well as in 5-HT content and number of uptake sites (Ricaurte et al., 1980). The effects of chronic cocaine on serotonergic functioning are less well established. For example, Ho and colleagues (1977) found decreased levels of 5-HT following chronic cocaine administration. Seiden and Kleven (1988). however, failed to find any effects of chronic cocaine on the biosynthesis of serotonin.

Some of these discrepancies can be reconciled by the fact that different chronic dosing regimens produce different changes in 5-HT systems. For example, Cunningham and colleagues found that daily injections of cocaine resulted in an increased sensitivity of dorsal raphe somadendritic 5-HT autoreceptors to cocaine's inhibitory effects as measured by electrophysiological techniques (Cunningham & Lakoski, 1988, 1990). These results are consistent with the behavioral data of King and colleagues (1993a), who found that daily cocaine injections produced an enhanced inhibitory effect of NAN-190 on cocaine-induced locomotion and an enhanced excitatory effect of 8-OH-DPAT on locomotion. In contrast with these results, the continuous infusion of cocaine via an osmotic minipump results in a decreased sensitivity of dorsal raphe somadendritic 5HT autoreceptors and a decreased excitatory effect of 8-OH-DPAT on locomotion (King, Joyner, & Ellinwood, 1993b; King et al., 1993a).

Interestingly, the depletion of 5-HT or reduction of 5-HT neurotransmission is associated with impulsive behavior. For example, Linnoila et al. (1983) found that violent offenders with a diagnosis of personality disorder associated with impulsivity had lower levels of 5-hydroxyindoleacetic acid (5-HIAA, the metabolite of 5-HT) than other offenders. After extensively reviewing the literature, Brown and Linnoila (1990) concluded that low levels of CSF 5-HIAA are related to disinhibition of aggressive/impulsive behavior and not to antisocial acts in and of themselves. The transition to

high-dose cocaine use might be considered impulsive behavior because the individual is focusing on the immediate, short-term advantages of drug consumption while ignoring the long-term advantages of drug abstinence. Hence, the 5-HT receptor supersensitivity, and resulting inhibition of 5-HT neurotransmission, may be a contributing factor to the development of the high-dose, bingelike pattern of cocaine abuse.

OPIATES

The opiates are derived from the poppy plant and have been used for centuries. A number of types of endogenous opiate receptors have been identified and their locations mapped. There are high concentrations of opiate receptors in the caudate nucleus, nucleus accumbens, periventricular gray region, and the nucleus arcuatus of medobasal hypothalamus (Pert, Kuhar, & Snyder, 1975, 1976). These areas may be differently involved in the reinforcing, aversive, and dependence-producing effects of the opiates. Furthermore, different receptor subtypes may mediate the different effects of the opiates.

The opiates produce analgesia, changes in mood (e.g., euphoria and tranquility), drowsiness, respiratory depression, and nausea (Jaffe & Martin, 1990). These drugs also reduce motivated behavior; there is a decrease in appetite, sexual drive, and aggression. Intravenous administration of opioids results in initial effects of flushing of the skin and sensations in the abdominal regions that have been likened to a sexual orgasm (Jaffe, 1990).

With continuous use of opioids, marked tolerance develops to some, but not all, of the effects of these drugs. Tolerance to opioids is generally characterized by a shorter duration of effect and attenuated analgesia, euphoria, and other CNS-depressant effects; however, there is less tolerance to the lethal effects of opiates. Therefore, if an individual administers ever larger doses to obtain the same effect (e.g., the rush or high), this may increase the probability of a lethal overdose (Jaffe, 1990).

Although the course and severity of withdrawal symptoms following opiate abstinence depend on which opiate was used, the dose and pattern of consumption, the duration of use, and the interdose interval, the opiate withdrawal syndrome follows the same general progression. Approximately 8 to 12 hours after the last dose, individuals experience yawning, lacrimation, and rhinorrhea; 12 to 14 hours after the final dose, they may fall into a fitful, restless sleep and awaken feeling worse than when they went to sleep. With the continuation of opiate withdrawal, they experience increasing dysphoria, anorexia, gooseflesh, irritability, agitation, and tremors. At the peak intensity of the withdrawal symptoms, they may experience exacerbated irritability, insomnia, intense anorexia, weakness, and profound depression. Common symptoms include alternating coldness and intense skin flushing and sweating, vomiting and diarrhea (Jaffe, 1990). This pattern of symptoms indicates that during the initial withdrawal phase there is a generalized CNS hyperexcitability. Thus, the addicted opiate abuser continues to recycle opiate use to both avoid or terminate the wtihdrawal symptoms, and to reexperience the euphoric effects. This powerful combination of euphoria, tolerance, and withdrawal can lead to profound levels of addiction.

Studies have found that rats and monkeys will self-administer opioids, thus indicating that these drugs serve as reinforcers (Koob & Bloom, 1988). Chronic opioid administration results in physical dependence, as demonstrated by the presence of a withdrawal syndrome following drug cessation. Most clinicians hold the classic position that physical dependence (i.e., avoidance of withdrawal symptoms) is a major motivating factor in opiate self-administration, but evidence indicates that reinforcement and withdrawal are separate processes. Bozarth and Wise (1984) demonstrated that rats will self-administer morphine into the ventral tegmental area without the presence or development of any apparent withdrawal symptoms. Chronic administration of morphine into the periaqueductal gray area, however, produces signs of a strong withdrawal syndrome.

Several lines of evidence indicate that dopaminergic neurotransmission may partially mediate the reinforcing effects of opiate administration. First, injection of met-enkephalin into the ventral tegmental area results in increases in DA release in the nucleus accumbens (Di Chiara & Imperato, 1988). Second, although opiates generally produce sedation, low doses of systemic morphine increase locomotor activity (Domino, Vasko, & Wilson, 1976). Third, injections of morphine into the ventral tegmental area

produce circling behavior (Holmes, Bozarth, & Wise, 1983); injections of opiates into the ventral tegmental area produce increased locomotion, as with systemic injections of opiates, thereby suggesting increased dopaminergic transmission (Blaesig & Herz, 1980). Fourth, selective lesions of the dopaminergic system decrease opiate self-administration, although not to the extent of affecting cocaine self-administration (Bozarth & Wise, 1985). Fifth, rats learn to self-administer opiates directly into the ventral tegmental area (Bozarth & Wise, 1984), rats also inject opiates into the nucleus accumbens and the lateral hypothalamus (Goeders, Lane, & Smith, 1984). Sixth, administration of the D1 antagonist SCH 23390, but not the D2 antagonists sulpiride and spiperone, block the reinforcing effects of morphine.

Ettenberg and associates (1982) found no effect of alpha flupenthixol, primarily a D2 antagonist, on heroin self-administration, although the same doses decreased cocaine self-administration. Similar results have been reported by others using other dopaminergic antagonists (DeWit & Wise, 1977). Thus, both place preference and self-administration procedures indicate that opiates are not reinforcing through D2 receptors, which are vital to stimulant reinforcement. These results indicate that opiate reinforcement is at least partially independent of the D2 stimulant type of reinforcement, yet they do act through a dopaminergic mechanism to induce a significant part of their effects.

Chronic administration of opiates produces several behavioral and neurochemical effects that may be related to their reinforcing effects. First, chronic administration of morphine results in the augmentation of the behavioral effects of low doses of morphine. In other words, subjects undergoing chronic opiate administration become sensitized to the behavioral effects of morphine (Ahtee, 1973, 1974). Second, chronic morphine administration results in decreased DA turnover in the striatum and limbic system during withdrawal (Ahtee & Attila, 1980, 1987). Third, in mice withdrawn from morphine, the synthesis and release of DA are attenuated (Ahtee et al., 1987); similar results have been obtained with human heroin addicts in which CSF homovanillic acid concentrations were decreased (Bowers, Kleber, & Davis, 1971).

These results indicate that during chronic morphine administration there is a down-regulation of the dopaminergic system and a neuroadaptation to this depletion. During withdrawal from opiate administration there is an augmentation of dopaminergic mechanisms. Indeed, during withdrawal rats are sensitized to the behavioral effects of apomorphine (Ahtee & Atilla, 1987), and small doses of morphine increase striatal homovanillic acid levels more in withdrawn than in control rats, thereby indicating that the dopaminergic system is sensitized at this point (Ahtee, 1973, 1974). Thus, some of the withdrawal symptoms (e.g., irritability and dysphoria) may be mediated by changes in dopaminergic functioning.

Acute administration of opiates increases the synthesis of 5-HT and the formation of 5-HIAA, and these effects are eliminated by the administration of opiate antagonists (Ahtee & Carlsson, 1979), thus suggesting that opiate administration results in increased serotonergic functioning. Indeed, acute administration of dynorphin-(1–13), while it decreases striatal dopamine, actually increases striatal serotonin (Broderick, 1987). This increased serotonergic functioning may contribute to the "post-consummatory calm" produced by opiate drugs: Increasing serotonergic functioning would tend to inhibit incentive-motivated behaviors and produce a calm, tranquil state. Indeed, the atypical anxiolytic drug buspirone exerts its anxiety-reducing effects via serotonergic activation.

During withdrawal from chronic opioid administration, 5-HIAA levels are decreased (Ahtee, 1980; Ahtee et al., 1987). This pattern of serotonin results could well cause increased impulsivity and a higher probability of relapse, similar to that described earlier in relation to the psychomotor stimulants.

In summary, like cocaine, the opiates are consumed because of their reinforcing properties. These reinforcing properties are the result of activation of endogenous opiate receptors; furthermore, activation of the dopaminergic system modulates the reinforcing effects of opiates. During chronic opiate administration, subjects become physically dependent. There is an increase in dynorphin levels that may mediate some of the aversive aspects of the withdrawal syndrome (e.g., decreased dopaminergic functioning). Furthermore, during chronic administration, there is functional down-regulation of both the dopaminergic and serotonergic systems. Upon withdrawal from opiates, there is a subsequent supersensitivity of the dopaminergic system. This

dopaminergic supersensitivity may be involved in opiate craving and general irritability during withdrawal.

See also **Addiction: Concepts and Definitions; Brain Structures and Drugs; Opioid Complications and Withdrawal; Research, Animal Model: An Overview; Tolerance and Physical Dependence; Wikler's Conditioning Theory of Drug Addiction.**

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GENDER

A consistent finding throughout many epidemiologic investigations in the United States and worldwide is that men are more likely to initiate, use heavily, and become dependent on alcohol and most forms of illicit drugs. Because of the pervasive way in which gender roles affect most aspects of people's lives, it remains a complex task to understand gender differences in patterns of drug and alcohol abuse. This section reviews the evidence for the following factors: 1) a biological basis for sex differences; 2) a social and psychological basis for gender differences; and 3) the narrowing of gender differences over time.

BIOLOGICAL BASIS FOR SEX DIFFERENCES

With regard to alcohol consumption and related problems, epidemiologic data within and across time and culture indicate that women drink less alcohol than men and have a lower overall prevalence of alcohol abuse and dependence than men. Two theories regarding the biologic basis for sex differences are genetic vulnerability and alcohol sensitivity. While early twin and adoption studies suggested greater genetic contribution to alcoholism among men, larger, population based twin samples show no sex difference in heritability. Thus it is commonly accepted that differences in genetic vulnerability do not explain the sex gap in alcohol use disorders. Other biological factors include male-female differences in alcohol metabolism and greater sensitivity to adverse health effects due to heavy drinking among women. Sex differences in the ratio of water to total body weight also cause differential metabolism of alcohol and drugs. This and other biological factors may cause women to have higher blood-alcohol concentrations (BACs) than men at equal dosages. This causes women to feel the ill effects of alcohol after a lower level of

consumption, possibly guarding against heavy alcohol consumption that can lead to symptoms of alcohol abuse and dependence.

Similarly, epidemiologic data indicate that men are more likely to be current illicit drug users, and have higher rates of drug abuse and dependence across specific substance. Some data on adolescents show limited gender differences in the rate of drug initiation, with adolescent females more likely to report nonmedical use of prescription drugs such as amphetamines. This pattern could be indicative of decreasing gender differences in drug and alcohol use seen within younger age groups, and the use of amphetamines for weight control that may be desirable for more young women than men. Clinical studies have indicated that women differ from men in the biological response to drug administration. Animal studies show that female rats have a higher behavioral response to cocaine administration compared to male rats but that the difference diminished following ovariectomy (removal of the ovaries). Human studies indicate that women report more anxiety after cocaine administration but less euphoria and dysphoria. Drugs that are deposited in body fat, such as marijuana, may be slower to clear in women than in men because of the higher proportion of body weight that is fat in women.

The path from first use to dependence also differs between men and women, although there is evidence that gender differences in these paths also decrease over time. Women who use alcohol and drugs often start using later than men, have a faster progression from first use to dependence, and enter treatment sooner than men given equal ages of dependence onset, although no such differences have been observed for crack-cocaine users. This phenomenon has been termed *telescoping*, although some evidence indicates that gender differences in the course of alcohol and drug abuse decrease over time. Further, despite drinking less alcohol than men and having a lower overall prevalence of alcohol abuse and dependence than men, women who drink have more alcohol-related problems compared to men who drink.

SOCIAL AND PSYCHOLOGICAL BASIS FOR GENDER DIFFERENCES

Social factors play an important role in the development of substance use disorders across gender, and thus the gender differences in social responses are implicated as the basis for the gender differences seen in substance use disorders.

In the early part of the twentieth century, alcohol researchers theorized that women were less likely to use alcohol and drugs because female sex roles were characterized by "conventionality" and the "acceptance of the dominant 'official' standards of morality and propriety" (Clark, 1967). Women who abstained from drugs and did not drink heavily were hypothetically following the official standards of morality and propriety for women in the time period, and since men were not bound by the same standards with regard to alcohol use, they were more likely to develop chronic alcohol problems. Evidence supporting this theory shows that more women strongly disapprove of a women getting drunk alone or at a party and further anticipate that they would be disapproved of for drinking heavily in public, compared to men. Further, both men and women are more likely to rate a woman who drinks while on a date as sexually aggressive compared to a man who drinks while on a date. Limited data on social stigma toward drug use exist, but existing literature shows similar if not stronger patterns of gender-related stigma. Stigma associated with drug and alcohol use across time and within subgroups of the population remains a rich area for future research.

Other work using gender roles to explain differences in substance use posit that there are distinctive gender styles in expressing pathology. Specifically, the male style features acting-out or externalizing behaviors (including drug and alcohol use), whereas the female style involves the internalization of distress. These distinctions are sometimes labeled "distraction" versus "rumination" (respectively), and have been extensively studied as mechanisms for an abnormal psychological response to stress (Nolen-Hoeksema & Harrell, 2002; Nolen-Hoeksema Larson & Grayson, 1999). However, comorbidity between depression and alcohol use disorders is often greater in women than men, above that which would be expected due to differing base rates of the disorders; additionally, evidence suggests no difference in affective disorder comorbidity between male and female cocaine-dependent patients but females are twice as likely to express an anxiety disorder. Taken together, these data suggest that the presence

of psychopathology may obscure traditional gender differences in response styles.

Sociological explanations for gender differences in alcohol and drug use include the hypothesis that stress among women due to the pursuit of both career and family leads to increased alcohol use and misuse. However, since other studies indicate that women with multiple roles are at lower risk for alcohol use disorders, this explanation seems unlikely. An association between the frequency of drinking among women and the number of men in their workplace was interpreted as showing an imitation effect. A study of medical students in the 1980s found that, at the start of medical school, female students had fewer alcohol-related problems than men, but by the start of clinical training, the gender difference had disappeared. Perhaps imitation as well as increased socialization to traditionally male medical roles decreased constraints against drinking shown by the women at the beginning of medical school.

DECREASING GENDER GAP IN SUBSTANCE USE DISORDERS

A wealth of epidemiologic data indicated that the gender gap in the initiation and use of alcohol and drugs was closing between 1998 and 2008 among adolescents and adults, providing support for the validity of sociological theories of the gender difference in alcohol and drug use disorders (as biological differences would not rapidly shift over such a short period).

Studies of adolescent substance use have consistently shown a convergence between males and females in the rates of alcohol and drug use initiation in younger birth cohorts, especially those born after World War II, and many studies of adults across culture indicate convergence in the rates of alcohol consumption. Several genetically informative samples have been studied with respect to sex differences in *DSM-IV* alcohol and drug use disorders over time, unanimously finding support for such a convergence. Similarly, large, representative, cross-sectional studies in the United States support gender convergence in rates of *DSM-IV* alcohol abuse and dependence. Furthermore, evidence indicates that the traditional telescoping phenomenon whereby women exhibit later onset of drug use and disorders but earlier treatment and shorter course may be diminishing, as women are more closely approximating men in both the onset and course of these disorders.

Many explanations for the gender differences have been proposed, although these theories are difficult to test empirically because they mostly rely on historical analysis. The increases in the proportion of women working outside the home and decreases in the proportion of women having children has been hypothesized to be a cause of the diminishment of many gender-based social norms, possibly including stigma associated with female drinking and drug use. Furthermore, changes in gender-based drinking norms have been documented between 1979 and 1990, indicating that although there was no change in the proportion of respondents who felt that "a man drinking at a bar with friends" was acceptable, there was a significant increase in the proportion that felt "a woman drinking at a bar with friends" was acceptable (Greenfield & Room, 1997). This finding indicates a decrease in the negative perception associated with drinking in women, potentially leading to greater opportunities to experience alcohol problems. Finally, changes in the opportunity to drink and alcohol advertising may have an effect on changing gender differences. For instance, from 2001 to 2002, the proportion of young girls exposed to print advertising of low-alcohol beverages (e.g., wine coolers) increased by 216 percent (Jernigan et al., 2004). These and other time trends in young women's exposure to alcohol advertising may have increased the social acceptability of drinking by women in younger generations.

In conclusion, despite a reduction in the gender gap regarding alcohol and drug use disorders, a robust difference remains. Some large scale epidemiologic data indicate that men are approximately three times more likely to have a current alcohol use disorder and a current drug use disorder (Hasin et al., 2007; Substance Abuse and Mental Health Services Administration, 2005). Regardless of a gender difference, however, alcohol and drug use disorders remain relatively common in both men and women compared to other psychiatric disorders, and drastically under-treated across gender as well. As gender norms continue to shift over time, people could see a further attenuation of the gender gap in the prevalence of disorders and/or new gender differences emerging in the onset, course,

and long-term effects of alcohol and drug use disorders. This area is important for continued monitoring and hypothesis testing to better understand the etiology of alcohol and drug dependence, as well as to develop effective treatment strategies for both men and women.

See also **Conduct Disorder and Drug Use; Epidemiology of Alcohol Use Disorders; Epidemiology of Drug Abuse; Gender and Complications of Substance Abuse.**

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GENETIC FACTORS

Substance dependence is strongly influenced by environmental factors, including the availability of the substance. However, substance dependence is also a familial and genetic disorder. Several lines of evidence demonstrate a substantial genetic component for the risk of substance dependence:

1. Alcohol dependence: Compared to the general population, siblings (brothers or sisters) of alcoholic parents have a 3- to 8-fold increased risk of developing alcohol dependence.
2. Drug dependence (including cocaine, opiates, nicotine, cannabis, hallucinogens, sedatives, and/or stimulants): Significant concordance rates between twin pairs shows a familial basis for different forms of drug dependence; the difference in pair wise concordance rates for monozygotic (MZ; i.e., identical) and dizygotic (DZ; i.e., fraternal) twins was significant for the abuse of marijuana, stimulants, cocaine, and all drugs combined. Because MZ twins share 100 percent of their genes and DZ twins share, on average, only 50 percent of their genes, a fully penetrant (expressed) genetic disorder should be twice as common in identical as in fraternal twins. For example, in one study, for stimulant (e.g., cocaine) abuse, the MZ twin correlation coefficient was 0.53 and for DZ twins it was 0.24. For opioid dependence specifically, the MZ twin correlation coefficient was 0.67 and the DZ correlation coefficient was 0.29 (Kendler & Prescott, 1998).
3. In genetics: *Heritability* is the proportion of phenotypic variation in a population that is attributable to genetic variation among individuals, reflecting the relative contributions of genetic factors to the total risk for a disorder (e.g., substance dependence). The heritability of substance dependence has been estimated from twin studies to be between 0.37 and 0.60, indicating that between 37 percent and 60 percent of the risk of substance dependence is due to genetic factors. For different types of substance dependence, the heritability has been found to be the following, in decreasing order: alcohol dependence (0.60), smoking persistence in males (0.59), smoking initiation in females (0.55), smoking persistence in females (0.46), smoking initiation in males (0.37), stimulant (including cocaine) abuse (0.44) and opioid dependence (0.43).

Findings from family studies show the familial trends in substance dependence, but environmental effects are unaccounted for in these studies. Findings from twin studies have shown a greater weight for the genetic components in these familial trends. Further, findings from adoption studies have decreased estimates of the contribution of environmental components to these familial trends. Together, these three kinds of studies provide evidence that genetic factors constitute a significant cause of substance dependence; in other words, a substantial part of the risk for substance dependence can be attributed to genetic variation.

GENE VARIATION AND DETECTION STUDIES

Gene variation could alter the density or affinity of proteins. Alteration of the functions of proteins may affect risk for diseases including substance dependence. Substance dependence is a genetically complex disorder that is multigenic, meaning that many genes contribute to risk for this disorder, with the effects of each risk gene being minor. These genes may act independently or may interact with each other or with environmental factors to generate additive or multiplicative effects on risk for substance dependence.

To detect risk genes for substance dependence, linkage studies, which detect the gene-disease relationship in families, and association studies, which detect the gene-disease relationship in unrelated cases and controls, are commonly performed. Usually, linkage studies using genome-wide scanning locate one or several chromosomal regions that are 10–20 million nucleotides wide and that may include dozens of genes. Association studies can

be used to locate more finely the specific risk variants in those genes. Genome-wide linkage studies have detected multiple risk regions for substance dependence. Risk regions for alcoholism include chromosomes 1, 2, 4, 6, 7, 8, 10, 12, 14, 16, and 17 (in mixed European-American [EA] and African-American [AA] samples). Genome-wide scanning located risk regions for cocaine dependence or cocaine dependence-related traits at chromosomes 10 (in mixed European-American [EA] and African-American [AA] samples); 3 and 12 (in EAs), and 9 and 18 (in AAs); risk regions for opioid dependence at chromosomes 17 (in EAs and AAs) and 2 (in AAs); and eight risk regions for nicotine dependence at chromosomes 2, 4, 9–12, 17, and 18 in EAs, and 9–11 and 13 in AAs. Association studies, which mostly were based on hypothesized effects based on candidate genes (i.e., those involved in processes that have been shown to be important to the development of maintenance of substance dependence), have detected many risk genes for substance dependence (especially alcohol dependence), among which consistent and replicable findings mainly include a dopamine receptor D2 gene (DRD2); kinase-domain-containing gene (ANKK1); alcohol dehydrogenase genes (ADHs); aldehyde dehydrogenase genes (ALDHs); gamma-aminobutyric acid (GABA), type A receptor alpha 2 gene (GABRA2); mu-opioid receptor gene (OPRM1); a cannabinoid receptor gene (CNR1), and a cytochrome P450 gene (CYP2E1). Positive findings have also been obtained for catechol-O-methyltransferase gene (COMT), ð-opioid receptor gene (OPRD1), κ-opioid receptor gene (OPRK1), muscarinic acetylcholine receptor M2 gene (CHRM2) and neuropeptide Y gene (NPY). There are many other genes showing association signals, but these findings are still very preliminary. Researchers are performing genome-wide association studies to search the risk genes for substance dependence, increasing the likelihood that more risk genes will be identified in the near future. By combining the positive predictive values of all risk genes identified to date, the total contribution of genetic factors to risk for substance dependence can be calculated and the risk of substance dependence predicted. Overall, environmental influences account for 42 to 52 percent of the risk for substance dependence, and genetic factors are estimated to contribute 48 to 58 percent of the risk.

GENETIC BASIS FOR THE CO-MORBIDITY IN SUBSTANCE DEPENDENCE

Different types of substance dependence often co-occur. For example, patients with alcoholism are 35 times more likely to have comorbid cocaine dependence than non-alcoholics, and are 13 times more likely to have comorbid opioid dependence than non-alcoholics (Regier et al., 1990). One possible cause of this high rate of co-morbidity is the synergic actions of different substances, such as alcohol, which enhances the effects of many drugs. For example, cocaine and alcohol are metabolized to cocaethylene, which has biological properties similar to cocaine but is longer acting. Many cocaine abusers therefore prefer to use cocaine together with alcohol, contributing to the high rate of co-morbidity of alcohol dependence and cocaine dependence. As another specific example, simultaneous systemic administration of both alcohol and nicotine results in an additive dopamine release in the nucleus accumbens (NAcc). This additive effect of alcohol and nicotine on the mesolimbic *reward pathway* may contribute to the high incidence of smoking in alcoholics. A second possible cause of the high rate of co-occurring substance dependence is a shared mechanism in the development of dependence on various substances. Several types of substance dependence share common features, including symptomatology, neuropsychological impairments, pathogenetic mechanisms, and response to specific treatments (e.g., the effects of disulfiram, an ALDH blocker, which was approved for the treatment of alcohol dependence, has also been shown to be efficacious in the treatment of cocaine dependence). Many studies have also demonstrated that different types of substance dependence may share susceptibility genes; for example, OPRM1 gene variation was found to moderate susceptibility to alcohol dependence and/or drug dependence; in some studies DRD4 gene variation was found to be related to alcohol dependence and/or drug dependence; multiple ADH genes, multiple OPR genes, the CHRM2 gene, and the CNR1 gene were associated with both alcohol dependence and drug dependence; and finally OPRM1 and CHRNA4 have been reported to be associated with both nicotine dependence and alcohol dependence. These common features and shared susceptibility genes suggest that various types of substance dependence have common developmental

mechanisms. It is possible that the dopaminergic signaling pathway that plays a role in reward and reinforcement may be the final common pathway in the development of various types of substance dependence. Although various types of substance dependence may have similar mechanisms, these mechanisms probably do not overlap completely. The similarity and specificity of the mechanisms for different subtypes of substance dependence continue to be under investigation.

GENETIC MARKERS: RISK GENES FOR SUBSTANCE DEPENDENCE

Usually, the genotype frequency distribution of a single gene marker displays a balance in the general population; this is known as the Hardy-Weinberg Equilibrium (HWE). This equilibrium in regard to risk markers can be absent in what is known as the Hardy-Weinberg Disequilibrium (HWD), by certain causes, such as disease. Many studies have found that a number of genetic markers were in HWD in the sample with substance dependence, but in HWE in healthy subjects. This suggests that these markers are inherited in a recessive manner. These markers have been found in multiple ADH genes, multiple OPR genes, the CHRM2 gene, and probably in additional genes, suggesting that the mode of inheritance of risk genes for substance dependence may differ substantially from those for other mental illnesses.

Different populations have different generations of ancestry; for example, the African population is much older than the European population. This difference may result in different rates of decay of linkage disequilibrium (LD; correlation between two genetic markers) from the initial generations to the current generations. Although several markers in strong correlation often form an LD block, different rates of decay of LD are one factor that results in different LD block sizes between populations. Some populations could have broader LD blocks (i.e., more markers located in one block) than other populations; this leads to population-specificity of associations between genes and diseases. For example, many associations between ADH genes, ALDH2 genes, and alcohol dependence have been reported in some populations, but not in others. Due to genetic drift or selection, different populations may also have different allele frequencies at the same locus, which also leads to population-specificity of associations between genes and diseases. To generalize the associations, replication studies in different populations is extremely important in research on the genetics of substance dependence.

PERSONALITY TRAITS AND SUBSTANCE DEPENDENCE

Personality traits play an important role in the genetics of substance dependence. There are three hypotheses concerning relationship between genes and personality as risk factors for substance dependence:

1. Genes bridge the association between personality and substance dependence. Common genetic factors may largely underlie the association between personality traits and substance dependence. For example, 70 percent of the association between antisociality and alcohol dependence can be explained by common genetic factors. In addition, alcohol dependence and conduct disorder share many personality traits that may be accounted for by common genetic risk factors. There is also direct evidence that personality traits and substance dependence are linked to polymorphisms in the SLC6A4 gene (which encodes the serotonin transporter), the OPRM1 gene, the ADH4 and ADH7 genes, and the CHRM2 gene. These findings support the theory of a shared genetic basis for personality features and substance dependence; personality traits might have some underlying neurobiological mechanisms that also influence risk for substance dependence.
2. Personality bridges the association between genes and substance dependence. Personality traits may play a central role in the development of substance dependence. Specifically, some pre-morbid personality traits (i.e., those existing before the onset of substance dependence), such as *behavioral undercontrol* (including impulsivity, thrill seeking, rebelliousness, irresponsibility, nonconformity, and aggressiveness), rejection of societal values, antisocial behavior, and hyperactivity, are robust predictors of alcohol dependence. As postulated by many investigators, personality traits could be a substantial heritable component of substance dependence, serving as an intermediate phenotype for substance dependence. In other words,

certain personality traits are inherited and increase the likelihood that subjects who have them will develop substance dependence or substance dependence-related disorders. Thus, personality features may be more clearly genetic in origin than substance dependence *per se*, personality could be a genetically determined risk factor for substance dependence, and the more sensitive gene-personality association study designs could reasonably be used to detect and predict gene-disease associations.

3. Substance dependence bridges the association between personality and gene. It has been argued that personality traits, especially *negative emotionality* (anxiousness, inhibition, moodiness, and unhappiness), may be a consequence (or a secondary phenomenon) rather than a cause of substance dependence. Here, personality serves as an endophenotype (components in the pathway between disease and genotype that are measurable, but not readily apparent) of substance dependence. In short, the association between personality and gene can be attributed to the association between substance dependence and gene.

CURRENT CONTROVERSIES

Substance dependence is multigenic, and thus its etiology is extremely complicated. Researchers have been trying to quantify the relative contributions of genetic and environmental factors to the risk of substance dependence, but the exact ratio of such contributions between these two factors remains under investigation. The genetic effects are population-specific, and the designs vary between different studies, which make many findings difficult to replicate and conclusions controversial. High rates of co-occurrence of different types of substance dependence also complicates these studies because the causes for different types of substance dependence could be shared or independent. Thus, any investigation of a single type of substance dependence needs to be carefully designed. Additionally, the relationships among substance dependence, personality traits, and genes are complicated, and the true associations among them remain unclear. More research is needed in this area. Many hypotheses have been proposed to explain the mechanisms by which genetic variation affects the risk for substance dependence, but much work remains to be done. Finally, because substance dependence is not influenced by a single gene exerting a large effect (in contrast to, for example, Huntington's Disease), its mode(s) of genetic inheritance (e.g., dominant or recessive) are difficult to derive, a fact that hampers researchers who seek to understand the etiology of substance dependence.

See also **Complications: Mental Disorders; Conduct Disorder and Drug Use; Epidemiology of Drug Abuse; Women and Substance Abuse.**

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XINGGUANG LUO

LEARNING

Learning factors in substance abuse have received much attention. Two basic learning mechanisms are involved when an organism repeatedly self-administers a psychoactive substance. First, classical conditioning is engaged when environmental stimuli are associated with, and come to signal, the upcoming effects of the drug. Second, operant conditioning occurs as an organism learns that particular behaviors lead either to a drug reward or to punishment. The effects of these two processes presumably interact and influence repeated drug use and/or relapse to drug use following a period of abstinence.

Classical conditioning occurs when an organism makes an association between two events in the external environment. A typical classical conditioning situation involves learning that a biologically neutral event (the conditioned stimulus [CS], such as a familiar drug dealer) signals the upcoming occurrence of a biologically relevant event (the unconditioned stimulus [US], such as the effects of a drug). As a result of this signaling, the CS produces conditioned responses (CRs), which are related to the US and unconditioned responses (URs). A number of investigators have reported that CRs are elicited in humans by environmental events that signal upcoming drug use or withdrawal (Berger et al., 1996; Payne, McClernon, & Dobbins, 2007; Bordnick et al., 2008). Consistently, CRs to drug-related stimuli play a major role in maintaining drug-taking behavior (Sinha & Li, 2007).

Operant conditioning involves learning about contingencies between behaviors and their outcomes. A typical operant conditioning situation sets up contingencies between three different events: a response (e.g., inhalation of the drug), the outcome of that response (e.g., the reinforcing drug effects), and the stimulus situation in which that response-outcome relationship is established (i.e., the discriminative stimulus). Drugs of abuse function as potent reinforcers for human substance abusers, as evidenced by the fact that a variety of behaviors are directed toward their attainment and use. Consequently, understanding how operant behaviors directed toward drug reinforcers are acquired is critical to understanding human substance abuse and dependence.

Classical and operant conditioning may both be active during drug seeking and self-administration. Events that have consistently signaled drug use may eventually come to evoke CRs in the form of

craving—urges to use the drug. In this way, signals of drug use may motivate the drug user to initiate drug-seeking behavior. For example, walking past someone smoking a cigarette might act as a CS for a heavy cigarette smoker, evoking the craving for nicotine. This craving might then increase the likelihood of purchasing and smoking a cigarette (the reward).

OPERANT CONDITIONING WITH DRUG REINFORCERS

A large body of data shows that many drugs abused by humans act as reinforcers for animals in operant-conditioning situations. In typical studies on the reinforcing properties of drugs, rats or monkeys are fitted with venous catheters through which a drug can be administered directly. The animal's response, such as pushing a lever, results in infusions of the drug.

These studies have found that many drugs abused by humans—including cocaine, morphine, heroin, amphetamines, pentobarbital, and alcohol—establish and maintain operant behaviors in animals. Other drugs that are typically not abused by humans—such as aspirin, antidepressants, hallucinogens, and opioid mixed agonists/antagonists—do not cause a response (Gold & Balster, 1991; Hoffmeister & Wuttke, 1975).

The degree to which a drug reinforces behavior depends more on the schedule of reinforcement than on the drug itself. A schedule of reinforcement refers to how often a drug is given. For example, ratio schedules require a certain number of responses before a reinforcer is given. Interval schedules are set up so that reinforcers occur only after a certain amount of time has passed. Reinforcers in ratio schedules depend solely on the number of responses made; therefore, these schedules typically result in higher response rates than interval schedules in which responses made too early are ineffective. Because reinforcement schedules largely determine the response rate in a given situation, the abuse potential of the various drugs cannot be reliably assessed by comparing how quickly participants respond for each substance.

One technique used to compare the reinforcing properties of various substances involves calculating a *breaking point* under a progressive ratio schedule of reinforcement. A progressive ratio schedule requires a participant to make an increasing number of responses (the ratio) for each additional reinforcer. For a given drug dose, the breaking point is reached when the ratio becomes too high to support responding. This breaking point value then shows that drug's reinforcing properties, or *reinforcing efficacy*. Drugs with the highest breaking point are the most reinforcing and, hence, have the highest abuse potential. Of drugs studied using this procedure with animals, cocaine has the highest breaking point (Wang & Woolverton, 2007; Lile et al., 2005). Although there are no published laboratory data comparing the reinforcing efficacy of drugs of abuse in humans, a growing database indicates that several drugs—including cocaine and heroin—are self-administered by humans under progressive ratio schedules of reinforcement (e.g., Haney et al., 1998; Comer et al., 1999).

Choice experiments can also compare the reinforcing properties of different substances. Participants choose between two responses, each leading to different commodities (e.g., drug A vs. drug B, or a drug vs. a non-drug option). A preference for one response indicates a preference for the substance, or commodity, associated with that response. Data collected using choice procedures indicate that the choice to self-administer drugs of abuse is influenced by many factors, including dose, schedules of reinforcement, and magnitude (size or amount) of the other choice. There is a good correspondence between findings obtained for animals and for humans in choice experiments. For example, S. Stevens Negus (2003) found that monkeys self-administered less cocaine when the magnitude of the alternative reinforcer (number of food pellets) increased. Similarly, human cocaine self-administration decreased as the value of the monetary alternative increased (Higgins et al., 1994).

In sum, a body of both animal and human data now exists that documents the way drugs of abuse can act as potent reinforcers. The pattern of drug use exhibited by an individual user, however, appears to depend as much on the schedule of drug availability as on the particular properties of the chosen drug or on the presence or absence of other reinforcers. Therefore, predicting human patterns of drug taking will require a better understanding of drug availability in the real world.

CLASSICAL CONDITIONING OF DRUG-RELATED CUES

A number of investigators have suggested that stimuli previously paired with drug use (e.g., paraphernalia) or that reliably signal drug use (e.g., meeting the drug dealer) become CSs, which elicit CRs. In turn, this relationship (CS-CR) increases the likelihood of further drug use.

Conditioned Withdrawal Model. Abraham Wikler (1973) described unpublished observations supporting this perspective, in which he administered multiple daily doses of morphine, methadone, or heroin to research participants who were previously heroin-dependant and had undergone detoxification, inducing opioid dependence. Subsequently, irregular single doses of the opioid antagonist nalorphine consistently led to withdrawal (i.e., the unpleasant symptoms experienced by drug abusers following the abrupt cessation of drug use). Wikler occasionally substituted saline for nalorphine, evoking less severe withdrawal symptoms. While this supported the role of conditioning factors in opioid withdrawal, a more systematic evaluation in humans is clearly needed.

CONDITIONED TOLERANCE MODEL

A second model using conditioning was put forth by Shepard Siegel (1975; 1979). He proposed that stimuli paired with drug use evoke conditioned compensatory responses, which oppose the direct effects of the drug. As these drug-opposite responses increase over repeated conditioning experiences in the same environment, they increasingly oppose the effects of the drug. Therefore, abusers become tolerant to drug-related effects and find that, over time, they need larger doses to achieve a given effect. Accordingly, tolerance should decrease when drugs are administered in novel environments where CSs are not present. Of course, a plethora of data demonstrates the development and maintenance of drug tolerance in stable drug-taking situations, but the mechanism(s) underlying this phenomenon are multiple and complex. Only additional research can clarify the role conditioning plays in the developing drug tolerance.

Nevertheless, according to Siegel's theory, drug-related cues in the absence of drug-taking produce drug-opposite responses that are not canceled by the direct effects of the drug. These drug-opposite responses represent what the user experiences as withdrawal symptoms. Viewed from this perspective, conditioning can motivate drug use in two ways. First, the withdrawal symptoms following a period of abstinence can lead to drug use aimed at relieving these unpleasant effects. Second, tolerance to the effects of a drug may motivate a user to increase his or her level of use to maintain a fixed level of desired effect.

Siegel's model has not gone unchallenged. The primary objection to it is that CSs do not always produce drug-opposite responses. Instead, CSs sometimes produce responses that resemble the direct effects of the drug (e.g., euphoria), and may motivate drug use as well. Indeed, whether CRs produced by drug-related stimuli are drug-like or drug-opposite has not been determined, and some researchers have asserted that rather than drug-opposite responses, the memory of drug-induced euphoria is the major factor in continual drug use and relapse (e.g., Grant et al., 1996).

CONDITIONED INCENTIVE MODEL

Jane Stewart and colleagues (1984) have proposed that conditioned drug stimuli provide the impetus for further drug use by eliciting CRs that mimic the drug effects, which whet the appetite of the user. Such CRs are positively reinforcing and may lead to drug use by prompting the user to anticipate the pleasurable consequences of drug taking.

Some evidence for this model lies in the observation that many animals show drug-like responses to stimuli paired with drug use. This is particularly evident with stimulant drugs such as cocaine or *d*-amphetamine, as these drugs exhibit high abuse potential. Furthermore, researchers have found that animals that have stopped responding for a drug reinforcer may resume responding following a small unearned dose of the drug (a priming dose) and, importantly, that environmental signals for drug use may act in the same way as these priming doses (de Wit & Stewart, 1981). Some research suggests that CSs, paired with a reinforcing US, release dopamine (DA) in the brain's supposed "reward pathway" (Stewart et al., 1984; Schultz et al., 1998). Other research suggests that the contribution of multiple brain structures (e.g., amygdala, hippocampus, orbitofrontal cortex) and other neurotransmitters,

including glutamate and GABA, underlie priming-induced drug seeking.

These three conditioning models similarly propose that events paired with drug use become conditioned stimuli that, upon future presentation, encourage the drug user to initiate drug-seeking behaviors. The models differ only in the characterization of the CRs elicited by the drug-related events.

HUMAN DATA

Since the 1970s investigators have collected data from a number of sources to document that stimuli associated with drug use in humans is conditioned. Evidence for this has come from three primary sources:

- Self-reports by drug abusers about the conditions under which they experience craving and withdrawal.
- Attempts to establish drug conditioning in the laboratory.
- Assessments of responses to cues thought to be drug CSs in the natural environment (in cue-exposure paradigms).

Self-reports of Conditioned Effects. Many drug abusers report drug craving and withdrawal when faced with drug-related stimuli in their home environment or in the laboratory. Several investigators have systematically documented this in response to stimuli associated with a wide range of drugs, including alcohol, cocaine, heroin, and nicotine. It has been more difficult, however, to establish a link between subjective reports of craving and/or withdrawal and drug use. Recently, Rajita Sinha and colleagues (2006) studied outpatient cocaine abusers who had recently completed drug treatment. They found that cocaine craving was predictive of relapse and that stress-induced cocaine craving was a particularly important factor. Similar findings were found for self-reported methamphetamine craving in an outpatient treatment setting (Hartz et al., 2001). Such reports support the idea that events that signal drug self-administration in the home environment can cause conditioned responses of craving, which motivate further drug use.

Laboratory Conditioning Studies. Richard Foltin and Margaret Haney (2000) found that neutral stimuli paired with cocaine administration elicited conditioned physiological (e.g., increased heart rate and blood pressure) and subjective (e.g., cocaine craving) responses. A number of other studies using neutral stimuli paired with alcohol, nicotine, and opioids also reported similar effects brought about by the experimental CSs. Interestingly, Raymond Niaura and colleagues (1989) found that such physiological responses to a laboratory-presented CS predicted relapse to cigarette smoking 90 days later.

Laboratory studies show that such conditioning occurs as a consequence of experienced users taking drugs. However, the connection between potential CSs, drug effects, and CRs in the natural environment is undoubtedly less precise than in the laboratory.

Cue-Assessment Studies. To determine whether events associated with previous drug use in the natural environment acquired conditioned properties, many studies have recreated/presented typical CSs in the laboratory and measured participant responses. In such studies drug-dependent participants are exposed to drug paraphernalia or to audiotapes, videotapes, and photographs with drug-related content (i.e., "drug cues"), while physiological and self-report responses are obtained. Responses to such drug cues are then compared with the responses participants make when they are exposed to comparable stimuli lacking a drug-specific content.

Consistent with conditioning models, exposure to drug cues seems to produce CRs. Specifically, exposure to drug cues produces subjective reports of drug craving as well as other physiological changes (e.g., decreases in skin temperature and increases in heart rate; for review, see Carter & Tiffany, 1999). Data from imaging studies indicate that DA-rich brain structures, including the ventral tegmental area, ventral striatum, and prefrontal cortex, are activated when substance-dependent individuals are presented with drug cues (Volkow et al., 2006; Sinha et al., 2007). This suggests that DA may be involved in establishing conditioned responses to drug cues. In line with this view, S. Paul Berger and colleagues (1996) demonstrated that haloperidol, a DA

antagonist, significantly reduced cocaine cue-induced anxiety and craving.

Although drug cues have repeatedly increased drug self-administration in laboratory animals (e.g., de Wit & Stewart, 1981; Epstein et al., 2006), there is a dearth of parallel data collected using humans. In one study Payne and colleagues (1991) exposed tobacco smokers to highly salient smoking cues and found that cue exposure shortened the time participants took to smoke their first cigarette and increased participants' puff duration. Because the assumption that responses to drug-related stimuli motivate actual drug use is central to learning models, more studies using drug taking as a dependent measure are clearly needed.

CLASSICAL/OPERANT CONDITIONING INTERACTION

Although much evidence suggests that psychoactive drugs of abuse have powerful reinforcing properties—and that stimuli associated with those drugs elicit conditioned responses—the question remains as to whether these classically conditioned responses actually motivate drug-seeking behaviors by themselves. Indeed, much of the work on drug conditioning contains the implied notion that classical and operant learning effects combine to motivate drug use (or drug craving, even if no drug use actually occurs). The most common idea is that CSs evoke craving and/or withdrawal states, which motivate subsequent drug-seeking behaviors (via classical conditioning). In cases in which a drug is consumed, the effects of the drug further reinforce the drug-seeking behaviors (via operant conditioning).

TREATMENT IMPLICATIONS

If classical and operant conditioning motivate drug use, then substance-abuse treatments should aim at reducing the impact of these learning effects. The most commonly discussed interventions include aversion training, extinction, and behavioral and cognitive-behavioral alternatives.

Aversion therapy involves teaching drug abusers that those stimuli and responses that once led to positive drug effects will henceforth lead to unpleasant outcomes. The most common technique has been to pair self-administrations of a drug with pharmacologically induced sickness (e.g., the medication disulfiram can cause a variety of unpleasant and uncomfortable effects when followed by the ingestion of alcohol). While disulfiram may prevent alcohol consumption in the short-term, patients are unlikely to continue to self-administer disulfiram outside the treatment setting. Further, since the treatment setting is clearly different from the home environment, drug abusers may simply learn that drug-taking behavior is reinforced at home, but punished in the clinic. In general, disulfiram is ineffective in achieving alcohol abstinence or delaying relapse (Fuller et al., 1986), although it has been useful for patients who are older, highly motivated, and more socially stable (Fuller & Gordis, 2004).

Extinction training consists of repeatedly exposing drug abusers to drug-related stimuli without letting them take drugs. This breaks the association between these stimuli and the effects of drug use. Extinction of classically conditioned stimuli typically requires drug abusers to repeatedly view drug-related scenes, imagine scenarios, and handle paraphernalia without using the abused substance. Such training has the advantage of not subjecting the drug user to punishment. Operant extinction procedures require participants to repeatedly perform drug-use behaviors in the absence of a drug reinforcer. This can be accomplished by having participants administer their drug of abuse in the usual way—while they are maintained on a medication that blocks the effects of the abused drug (e.g., the opioid-blocking drug naltrexone). In this way drug-use behaviors are not reinforced as the drug effects are absent or considerably weakened. Nevertheless, participants might give up the drug in the clinic, but still experience conditioned effects that lead to drug use at home.

Cognitive-behavioral training also reduces the impact of conditioning on behavior. Subjects are taught to identify and avoid drug-related situations and to make different responses in the presence of drug cues (Sholomskas et al., 2005). These new responses compete with drug-seeking behaviors elicited by drug cues. Rather than trying to eliminate the craving produced by drug cues, this treatment gives the patient ways to avoid cues along with alternative behaviors and strategies to replace drug use as well as general coping skills. Behavioral alternatives to drug use range from simple time-outs, to forming images inconsistent with drug use, to

acting in ways that reduce the chances of use or cue exposure (e.g., going out to eat with non-drug-using friends). Cognitive strategies include changing expectations about drug use and considering long-term consequences of behavior. Taken as a whole, these approaches are now commonly designated as cognitive therapies or relapse-prevention approaches. The advantage of these procedures over aversion therapy and extinction is that patients use their training in the clinic to deal with high-risk situations in the real world.

Contingency management is another behavioral approach used to treat substance abuse. It has generated increased interest in recent years because it has produced consistent reductions in drug-using behaviors among diverse substance-abusing populations (Higgins et al., 2004). In this approach, individuals receive immediate rewards (e.g., cash or vouchers redeemable for goods or services) for providing drug-free urine samples, and the value of the rewards increases with consecutive drug-free urine samples. However, rewards are withheld if the patient's urine sample tests positive for an illicit drug. In addition to receiving rewards, drug abusers participate in cognitive sessions similar to those described previously, where they learn a variety of skills to help them minimize substance use. One problem with contingency management is that it may be too expensive for less well-funded treatment programs. Whether these particular conditioning interventions provide lasting help to substance abusers remains to be seen, but data suggest that in alcohol-, cocaine-, nicotine-, and opioid-dependent individuals, these cognitive and behavior techniques reduce the probability of relapse.

See also **Addiction: Concepts and Definitions; Conditioned Tolerance; Treatment, Pharmacological Approaches to: Naltrexone; Wikler's Conditioning Theory of Drug Addiction.**

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PERSONALITY

Clinicians and researchers alike have long posited that personality plays an important role in the etiology of substance use disorders (SUDs). Although empirical research has failed to identify a unique constellation of traits equivalent to a so-called addictive personality, a substantial body of research points to a few important traits that appear to put one at risk for developing SUDs, in particular, traits related to the tendency to experience negative emotions—e.g., neuroticism or negative emotionality—and traits related to self-control—e.g., impulsivity, sensation seeking, behavioral undercontrol (see Sher et al., 1999, for a review). Observing a statistical association between these traits and SUDs is not the end point of research on personality and SUDs but, rather, a starting point that helps to identify distinct etiological processes which contribute to the development of SUDs. Accumulating research suggests that personality is associated with multiple, distinct etiological pathways and indexes, core dimensions of individual vulnerability to SUDs that are heritable. Most, though certainly not all, research suggests that some traits represent vulnerability to a range of SUDs. However, even in the context of a general vulnerability to SUDs, it appears that some traits may differentially predispose an individual more to one type of SUD (e.g., alcohol dependence) than another (e.g., tobacco dependence).

DEFINING PERSONALITY AND IDENTIFYING ITS DIMENSIONS

Although various definitions of personality exist, most formal definitions state that personality is, as suggested by Watson and colleagues, "internal, organized, and characteristic of an individual over time and situations. . .[and has] motivational and adaptive significance" (1994, p. 18). Of particular relevance to research on addiction are *general factor models* that attempt to comprehensively map the major dimensions of adult personality (Watson, Clark, & Harkness, 1994). Typically, these models focus on either three major dimensions (known as the Big Three) or five (the Big Five).

Big Three models of personality reduce it to three dimensions, often labeled as neuroticism/negative emotionality, impulsivity/disinhibition, and extraversion/sociability. Neuroticism/negative emotionality includes facets such as anxiety, depression, guilt, stress reactivity, and emotionality. Extraversion/sociability includes liveliness, surgency, and social closeness. Impulsivity/disinhibition (often called behavioral undercontrol in the substance use literature) includes nontraditionalism, embracing risk, and impulsivity. More generally, behavioral undercontrol describes a broad range of behaviors that collectively reflect difficulty in inhibiting behavioral impulses (Elkins et al., 2006). It is important to note that some early-twenty-first-century work (Smith et al., 2007; Whiteside & Lynam, 2003) has utilized factor analyses to identify four distinct personality facets associated with impulsive-like behavior: sensation seeking, lack of planning, lack of persistence, and urgency (acting rashly when distressed).

Big Five models of personality include neuroticism (N), extraversion (E), openness to experience (O), agreeableness (A), and conscientiousness (C). In Big Five models, neuroticism and extraversion correspond to the similarly named traits in most Big Three systems. Agreeableness includes altruism, compliance, and modesty. Conscientiousness includes competence, achievement striving, and deliberation (and is closely related to, but not isomorphic with, impulsivity/disinhibition in Big Three systems). Depending on the specific form of the Big Five model being considered, the fifth dimension is sometimes referred to as either openness to experiences (Costa & McCrae, 1992) or intellect (Goldberg, 1990). The Big Three and Big Five models of personality appear to represent replicable structures of personality across diverse cultures, can serve as useful structures to examine the relationship of personality with SUDs (Sher et al., 1999), and may be integrated with some success (Watson et al., 1994).

PERSONALITY TRAITS AND SUDS

A number of personality traits have been associated with SUDs. As noted previously, it remains unclear if different personality traits predict different types of substance dependence. Some research suggests that personality traits, such as neuroticism/negative emotionality and disinhibition/impulsivity, correspond to the increased use and misuse of a number of substances, such as alcohol, tobacco, and illicit drugs (e.g., Sher et al., 1995). However, other research suggests that different personality traits predict different types of SUDs (e.g., Sher, Bartholow, & Wood, 2000).

To determine which personality traits predict alcohol, drug, and tobacco dependence symptoms and whether the strength of personality and SUD relationships differ by substance, Grekin, Sher, and Wood (2006) conducted a study in a large, longitudinal college student sample using well-validated factor models of personality. These researchers found that novelty seeking (a trait similar to behavioral undercontrol) and neuroticism predicted alcohol, drug, and tobacco dependence symptoms. These findings are consistent with previous research showing associations with SUDs and both disinhibition/impulsivity and neuroticism/negative affectivity.

However, these researchers also found that several personality traits were differentially related to alcohol, drug, and tobacco dependence symptoms. Specifically, alcohol symptomatology was predicted by low openness to experience and extraversion. Drug symptomatology was predicted by low conscientiousness, and tobacco symptomatology was predicted by low conscientiousness and openness to experience. These findings suggest that drug- and tobacco-dependent individuals have a less socially oriented, undependable personality profile than alcohol-dependent individuals.

In a similar study, Elkins and co-workers (2006) examined the association of personality at age 17 with the timing of onset and with the prospective prediction of nicotine, alcohol, and illicit drug disorders 3 years later in a twin sample. The earlier onset of alcohol and drug disorders (i.e., onset by age 17)

was related to low constraint (lack of behavioral inhibition and conventionality) compared to later onsets (i.e., onsets by age 20). High negative emotionality (the tendency to experience distress or anger) was related to the onset of either alcohol or drug disorders. Furthermore, the researchers found that low constraint and negative emotionality contribute uniquely (i.e., when adjusting for the other's contribution) and prospectively to the new onset of nicotine, alcohol, and illicit drug disorders, even when taking a past history of substance use into account. The authors conclude that the personality traits of low constraint and high negative emotionality represent a generalized risk for substance disorders during the peaks ages of onset during late adolescence and early adulthood.

In sum, nicotine, alcohol, and drug symptomatology appears to be related to impulsivity/low constraint and neuroticism/negative emotionality. Furthermore, alcohol-dependent individuals may have more socially oriented, dependent personality profiles than drug- and tobacco-dependent individuals. These findings suggest that core personality traits such as impulsivity/low constraint and neuroticism/negative emotionality increase the risk for developing any substance disorder, but some personality traits are more strongly linked with some substance disorders than with others.

MODELS OF THE RELATIONSHIP BETWEEN PERSONALITY AND SUDS

Observed associations between personality traits and SUDs suggest that personality variation is relevant to understanding substance abuse and dependence but does not necessarily inform us as to how or why personality contributes to the development and maintenance of SUDs. Existing literature suggests at least three etiological processes linking personality and SUDs (e.g., Sher et al., 1999; Sher & Grekin, 2007): (1) pharmacological vulnerability, (2) affect regulation, and (3) deviance proneness.

Pharmacological Vulnerability. The pharmacological vulnerability model posits that some individuals are pharmacologically predisposed to experience the effects of a substance in a way that increases their risk to engage in excessive consumption of the substance and/or to experience pronounced difficulties from the substance. Seemingly opposing predictions can be made from this model. For instance, it is hypothesized that individuals with *increased* sensitivity to positive or negative reinforcement from a substance are at an increased risk for a SUD because they receive a greater effect from the substance. However, it is also possible that individuals with *decreased* sensitivity to reinforcement use substances at larger amounts in order to achieve a desired effect, thus increasing their risk of physiological dependence.

Over the better part of the last century, there has been continual interest in the idea of personality traits influencing sensitivity to the effects of drugs. Several researchers (e.g., Claridge, 1967) have examined the effects of different drugs on behavioral performance and sedation thresholds (e.g., determining the dose of an intravenously administered barbiturate required to bring an individual to a predefined level of drowsiness) to test hypotheses of the relationship of drug effects to personality. These studies indicated that sensitivity to drug effects varied as a function of neuroticism and extraversion.

The rationales for these types of studies rely, in part, on neurobiological theories of personality positing that personality variation is a function of individual differences in the activity of major neurotransmitter and hormonal systems. Thus, drugs acting on these systems would be expected to have differential effects as a function of underlying (i.e., typical) variability in the activity of these motivationally important neurobiological systems. Alternatively, personality dimensions represent basic patterns of reacting to biologically meaningful stimuli, and thus individual differences in personality lead to characteristic responses to substances, such as alcohol, tobacco, and drugs. Research has indicated that individuals high in impulsivity/disinhibition appear to be more sensitive to the stress-reducing properties of alcohol, which is thought to make the effects of alcohol more reinforcing (e.g., Sher & Levenson, 1982).

Affect Regulation. It has long been recognized that individuals are motivated to use substances for a variety of reasons. Motivational theorists regard motivations as a gateway to substance use through which more distal influences, such as personality, are mediated (Cooper et al., 1995). Cooper developed and validated a four-factor model for drinking motivations among adolescents. Drinking motives were characterized along two underlying dimensions reflecting the valence (positive or negative)

and source (internal or external) of the outcomes an individual hopes to achieve by drinking. Crossing these two dimensions produces four classes of motives: (1) intrinsic positive reinforcement or enhancement (e.g., "How often do you drink to get high?"), (2) extrinsic, positive reinforcement for social rewards (e.g., "How often would you say you drink to be sociable?"), (3) intrinsic, negative reinforcement or coping (e.g., "How often do you drink because it helps you when you feel depressed or nervous?"), and (4) extrinsic, negative reinforcement to avoid social censure or conformity (e.g., "How often would you say you drink to fit in with a group you like?"). These motives have been extended to include motives for cigarette smoking, marijuana use, and other drugs.

Drinking for *positive reinforcement* or enhancement is strongly associated with personality traits related to reward seeking, and these motives have been shown to mediate the influence of personality on alcohol outcomes (Cooper et al., 1995). Theorists suggest that motivations for positive reinforcement from alcohol and other drugs of abuse are based on these substances' neuropharmacological effects on the brain centers involved in basic reward mechanisms.

On the other hand, *negative reinforcement* motives to drink are based on the hypothesis that alcohol and other drugs of abuse relieve negative affect. This self-medication or tension-reduction hypothesis has garnered considerable empirical support. Many people report that they drink to cope with negative affect, and these coping motives appear to mediate the effects of neuroticism/negative emotionality on drinking outcomes (Cooper et al., 1995). However, it is clear that not all individuals who have SUDs use substances to regulate affect, and there is considerable inter-individual variation in how effective various substances are in reducing negative affect.

Several things should be noted about the relationship between motives and personality. First, personality traits do not account for a high proportion of variance in substance use motives. Second, in several studies, the influence of personality on substance use outcomes still remains when controlling for motives, implying that mechanisms other than self-reported motivations are important in mediating personality effects on substance use. Consequently, although evidence exists that motivations act as a gateway to substance use through which more distal influences, such as personality, exert their effects, it is clear that additional mechanisms relate personality to substance use.

In addition, both correlational and experimental data support the mediating role of affect regulation on personality-substance use relations. The self-awareness model of alcohol (Hull, 1987) suggests that painful affective states, such as depression from a failure experience, are mediated by a state of self-awareness. Alcohol and other sedative/hypnotic drugs of abuse are thought to reduce this distress by disrupting the psychological mechanisms underlying self-awareness. Individuals with certain personality traits, such as high private self-consciousness (i.e., the trait counterpart of the state of self-awareness), are thought to be especially vulnerable to experiencing negative affect when presented with negative information about the self. Thus, these individuals are more likely to obtain relief from substances that reduce self-awareness when experiencing negative affect caused by self-awareness processes. Also, indirect evidence for the affect regulation model is based on the high comorbidity between SUDs and anxiety and mood disorders (Compton et al., 2007; Grant et al., 2004; Kessler et al., 1997; Hasin et al., 2007). Personality traits, such as neuroticism/negative emotionality, have been linked to both anxiety and mood disorders, and low extraversion/sociability appears to increase the vulnerability for depression (Clark, Watson, & Mineka, 1994). However, as noted above, not all individuals are likely to increase their substance use when anxious or depressed.

Deviance Proneness. The deviance proneness model posits that excessive substance use is not necessarily the result of physiological or psychological vulnerabilities to substances or the result of affective states. Rather, this model suggests that substance use is just one facet of a more general, deviant pattern of behaviors that originates in childhood and is the result of deficient socialization. These deficits are associated with a range of problem behaviors, such as a history of delinquent behaviors, childhood achievement problems, association with deviant peers, and substance use and abuse. Although a variety of theories exists on the relationship of these various problem behaviors to substance use, most view personality as an extremely distal influence, such

that personality is thought to influence long-term socialization processes created by parents and institutions in the community, such as schools. Other theories suggest that *risky* personality styles are associated with decision-making styles which are proximal to substance use (i.e., impulsive decisions surrounding substance use). It is important to note that these two models are not necessarily incompatible. For example, it is possible that personality affects substance use by influencing both peer group affiliations and risky decision making regarding substance use.

These three classes of models (pharmacological vulnerability, affect regulation, and deviance proneness) should not be viewed as exhaustive or mutually exclusive. Personality influences substance use through multiple pathways, although these pathways are largely theorized to be indirect and mediated by more proximal variables. However, the traitlike nature of personality makes it an important variable in the identification of individuals at future risk to develop SUDs.

PERSONALITY AND THE GENETIC RISK FOR SUDS

Some theories suggest that the genetic risk for SUDs is, in part, mediated by personality. It is believed that genetic factors account for individual differences in personality, with approximately one-third to one-half of the variation in personality attributed to genetics (e.g., Loehlin, 1992). Slutske et al. (2002) examined the extent to which the genetic risk for alcohol dependence and conduct disorder and their common genetic risk overlap with genetic factors contributing to a variation in dimensions of personality. These researchers found that genetic influences on personality dimensions accounted for a substantial proportion of the genetic risk for alcohol dependence. Specifically, behavioral undercontrol accounted for about 40 percent of the genetic variation in alcohol dependence risk, whereas negative emotionality accounted for a modest, yet significant, 4 percent of the genetic variation in alcohol dependence risk in men (but not women). Furthermore, the genetic influences contributing to variation in behavioral undercontrol accounted for about 90 percent of the common genetic risk for alcohol dependence and conduct disorder.

These findings suggest that genetic factors contribute to variation in dimensions of personality, which contribute to the risk for SUDs. In particular, behavioral undercontrol appears to be the personality dimension most strongly associated with alcohol dependence and explained the most genetic variation in alcohol dependence risk. Several theoretical models have been proffered to explain the causal link between genetically influenced variation in behavioral undercontrol and alcohol dependence (see above). Consistent with the deviance proneness model, higher levels of behavioral undercontrol may indirectly influence alcohol dependence risk (e.g., by leading to association with deviant, heavy-drinking peers), because it is associated with enhanced reinforcement from alcohol, or because of impaired decision making about drinking surrounding drug use.

PERSONALITY DISORDERS AND SUDS

Although traditionally there has been an interest in the role of personality in the development of SUDs, recent interest has turned to the comorbidity of SUDs and personality disorders (Compton et al., 2007; Grant et al., 2004; Hasin et al., 2007; Trull, Waudby, & Sher, 2004). *DSM-IV* personality disorders are composed of maladaptive personality traits. Thus, an interesting possibility raised by substance use and personality disorder comorbidity is whether this comorbidity is a function of the personality traits shared by both groups of disorders.

Trull and colleagues (2004) examined the relationships between major personality traits, *DSM-IV* personality disorder symptoms, and alcohol, tobacco, and drug use disorders. This study yielded two major findings. First, the relations between personality disorder symptoms (PDs) and SUDs were not completely explained by the covariation between PDs and SUDs and scores on major personality traits. Personality disorder symptoms predicted alcohol, tobacco, and drug use disorder diagnoses over and above the influence of major personality traits, including both Big Three and Big Five dimensions of personality. Second, the researchers found differential relations between personality disorder symptoms and substance use diagnoses. Symptoms of Cluster B personality disorders, which include antisocial, borderline, histrionic, and narcissistic personality disorders, were significant and unique predictors of alcohol and drug use diagnoses. Symptoms of Cluster A

personality disorders, which include paranoid, schizoid, and schizotypal personality disorders, were unique predictors of tobacco dependence. Differential relations among personality disorder symptoms suggest that different maladaptive personality traits are relevant to different forms of SUDs.

EFFECTS OF SUDS ON PERSONALITY

Although personality is typically viewed as a fixed trait that antedates the development of SUDs, for at least three decades it has been known that the development of SUDs can alter aspects of personality and the concept of pre-alcoholic or predependent personality characteristics is distinct from clinical alcoholic or dependent personality characteristics (Sher et al., 1999). This observation is based on the finding that several personality traits, especially those related to negative affectivity, tend to become less extreme over a period of abstinence in alcohol-dependent individuals. Neurobiological theories posit that adaptive strain imposed by heavy substance use on brain motivational systems (e.g., Koob & Le Moal, 1997) disrupts hedonic tone and contributes to a "downward cycle of addiction." In addition, over the course of development, a systematic change in personality occurs (Roberts, Walton, & Viechtbauer, 2006). Consequently, personality is probably less fixed than is typically assumed, changing systematically as a normal feature of development and, possibly, as a consequence of the dependence process itself (at least when the level of dependence is severe).

IN SUMMARY

Personality traits can be viewed as abiding, individual difference variables that play crucial roles in the development of SUDs. Existing research suggests that much of the genetic liability for SUDs is associated with a heritable variation in personality traits, and these traits may be etiologically important for multiple, and conceptually and empirically distinct reasons. For example, someone who is high on the broad trait of disinhibition may be vulnerable to substance dependence because he or she is more venturesome and likely to be exposed to substance use, may experience a bigger "kick" from a drug or simply enjoy altered states of consciousness more than average, and may have trouble inhibiting substance-using impulses (especially as dependence processes develop). Moreover, individuals who have SUDs are likely to have not only multiple SUDs but also a range of other psychological disorders (e.g., anxiety and mood disorders, or personality disorders) and these comorbid conditions can reflect, in part, the influence of personality. As dependence progresses, substance-induced disorders (i.e., transitory syndromes that are present only during and for a time after a period of active use) can develop and, presumably, reflect intra-individual personality change. Thus, the picture emerging from contemporary research is that personality is intimately linked not only with vulnerability to the development of SUDs but also with their course and in myriad ways. Although some differences clearly exist in the mean personality profiles of individuals with different forms of SUDs, in general, there are more similarities than differences in the personality risk for different SUDs. Indeed, certain constellations of personality traits (e.g., high neuroticism, low extraversion, low agreeableness, and low conscientiousness) appear to be risk factors for SUDs as well as psychopathology more generally (Trull & Sher, 1994).

See also **Conduct Disorder and Drug Use; Coping and Drug Use; Families and Drug Use; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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PSYCHODYNAMIC PERSPECTIVE

The psychological study and understanding of substance abusers has tended to be difficult, controversial, and complicated. Part of this contention derives from the nature of addictive illness; the acute (short-term) and the chronic (long-term) use of drugs and alcohol cause individuals to seem pleasure oriented, self-centered, and/or destructive to self and others, thus making them difficult to approach, understand, or treat. In other respects, the controversy or lack of understanding derives from competing ideas or schools of thought that debate (if not hotly contend) whether substance abuse is a disease or a symptom, whether biological and genetic factors are more important than environmental

or psychological ones, and/or whether substance abuse causes or is the result of human psychological suffering. Furthermore, during the final third of the twentieth century, psychological factors were minimized as researchers entered an era of biological psychiatry/psychology, in which empirical interest in brain structure and function (down to the microscopic and molecular level) predominated over interest in the person, the person's mind, and subjective aspects of human psychological life that govern both emotions and behavior. Although one cannot ignore that substances of abuse are psychoactive (powerful chemicals that act on the brain), there is a tendency to lose sight of the total person whose ways of thinking, feeling, and behaving (including subjective feelings about self and others) are equally and profoundly affected both by that chemistry and by the subjective effects produced by those psychoactive substances.

Clearly, biological, genetic (i.e., hereditary), and sociological factors are important in the development of drug abuse and dependence. Such factors, best studied by empirical methods, and modern technology have yielded new and valuable data since the late 1960s to explain aspects of addictive behavior. It is also noteworthy that during this period, clinical work with substance abusers has yielded data and findings of equal importance and validity, and this work has focused on some of the important subjective psychological factors that also explain aspects of addictive behavior, some of which empirical methods alone do not adequately explain.

This entry presents a psychological understanding of drug abuse and dependence based on the perspective gained from clinical work with alcoholic and drug-dependent individuals. In psychology and clinical psychiatry, it is referred to as the *case method* of study of human psychological problems. Guided by psychodynamic principles, this entry reviews what four decades of clinical work and case study with substance abusers has yielded on some of the main psychological influences that make likely or compelling the dependence on, and continued use and relapse to, drugs and alcohol.

ASSUMPTIONS

A psychodynamic perspective of human psychological life problems rests on the principle that people are all more or less susceptible to various forms of human psychological vulnerabilities; at the same time, they are also more or less endowed with human psychological strengths or capacities to protect against these vulnerabilities. Without ignoring hereditary factors, especially those that affect temperament, a psychological, and in this case psychodynamic perspective attempts to understand psychological forces at work (for example, drives and feelings) that operate within the individual at the same time that there is a corresponding interest in the psychological structures, functions, and defenses that observably (and just as often, less obviously) operate to regulate or control human drives, feelings, and behavior.

A psychodynamic approach to human psychology greatly depends on a developmental perspective or an appreciation of the psychological forces, structures, and functions as they develop and change over one's lifetime. Psychodynamic clinicians are especially interested in the way individuals are influenced in the earliest phases of development by parents (and other caregivers), and then in the development of relationships with other children and peers, and later in the life cycle in relationships with adults and small and large groups, all of which shape their life views and experiences, as well as their attitudes, values, and characteristic ways of reacting and behaving.

Based on these assumptions, clinicians have the opportunity, most usually in the context of treating patients, to study and understand how the degree of developmental impairments (or strengths) has predisposed toward (or protected against) psychological and psychiatric dysfunction, including addictive vulnerability. According to some clinicians modern psychodynamic-clinical approaches are as relevant and useful for studying and treating substance-dependent individuals as they are for the many other patients who benefit from them.

The psychological study and understanding of addictive illness necessarily requires the condition of abstinence (being free of drug/alcohol use). There is considerable debate about the duration of abstinence required before meaningful or valid psychological inferences can be made about individuals with addictive disorders. The confounding effects of acute and chronic drug/alcohol use are variable, and it is often surprising that within days or weeks—but certainly within several months of abstinence—how much can be learned about individuals' makeup and psychology that predisposed them to use and

become dependent on substances. This point about the requirement for a period of abstinence from drugs and alcohol is important to emphasize; otherwise, it can be and is rightfully argued that what appear to be the psychological causes of dependence on psychoactive substances are actually the result of such a dependence. Fortunately, in recent years, the combination of modern detoxification approaches, psychoeducational/rehabilitation/relapse prevention programs, twelve-step groups, and individual and group psychotherapeutic approaches, have been increasingly successful in establishing and maintaining abstinence. This result, in turn, has made psychological treatments and understanding increasingly possible.

PSYCHOLOGICAL SUFFERING AND SELF-CONTROL

A clinical-psychodynamic perspective suggests that human psychological suffering and problems with self-control are at the heart of addictive disorders. In fact, it is probably safe to say that to understand the psychology of addictive behavior is to understand a great deal about human psychological problems of suffering and control in general. The suffering that influences addictive behavior occurs at many levels, but it principally evolves out of susceptibilities involving individuals' self-esteem, relationships, emotions, and capacities to take care of themselves. Individuals who find various or particular drugs appealing (including alcohol) or who become dependent on them discover that, short-term, the drug action or effect relieves or controls their distress; that is, such drugs are used to self-medicate distress. Although problems with self-esteem and relationships are important parts in the equation of addictive behavior, it is mainly the problems with how substance-dependent individuals experience, tolerate, and express their feelings and their problems with self-care that makes addictive behavior so malignantly likely and compelling.

Problems with emotions and self-care painfully and repetitiously become involved with attempts to control suffering and behavior. This process includes such self-defeating coping patterns as impulsive actions and behaviors, psychological defensiveness (e.g., denial, boastful or arrogant postures, attitudes of invulnerability and toughness), and, ultimately, the use of drugs and alcohol. What originally is a solution for suffering and self-regulation—in which substances are used for relief or control—turns into a problem in which there is a progressive loss of control of one's self, the drugs or alcohol employed to combat one's difficulties, and possibly life itself.

THE SELF-MEDICATION HYPOTHESIS

The *self-medication hypothesis* specifically applies to some individuals who, by dint of temperament or developmental factors, experience and find that certain painful feelings (or affects) are intense and unbearable and that the specific action or effect of one of the various classes of abused drugs (e.g., analgesics, depressants, or stimulants) relieves their psychological pain and suffering. The self-medication hypothesis also implies that the particular drug or class of drugs preferred is not random. Rather, it is determined by how that class of drugs with its specific actions interacts with emotional states or particular painful feelings unique to the individuals who use or select their so-called drug-of-choice.

This is only one aspect of addictive suffering: Namely, emotions are experienced in the extreme, and addictive-prone individuals feel too much pain, so they resort to particular drugs to relieve their suffering. Another aspect of addictive suffering is that emotions are just as often absent, nameless, and confusing and that such individuals experience pain of a different type: They consciously feel too little of their distress and do not know when or why they are bothered (e.g., feeling empty, void, or cut off from emotions), and drugs or alcohol in these instances are used to change or control their emotions or suffering. In the first instance the operative motive is the relief of suffering; in the second, it is the control of suffering.

The self-medication hypothesis rests on the observation that patients, if asked, will indicate that they prefer or discover that one class of drugs has more appeal than another. Still, the drugs preferred by an individual are not the ones that are always used. Drugs that are actually used are just as often the result of other factors, such as cost and availability.

The three main classes of drugs that have been studied are the opioid analgesics (pain relievers), depressants or sedative-hypnotics (soothing, relaxing, or sleep-inducing drugs), and stimulants (activating or energizing drugs). The main appeal of opioids (e.g., heroin, morphine, oxycodone) is that

they are powerful subduing or calming agents. Besides calming or subduing physical pain for which they were originally intended, opioids are also effective in reducing or alleviating distressing or disruptive emotions. Beyond its calming influence on physical and emotional pain in general, however, the main and specific action of opioids, namely as an anti-rage or anti-aggression drug, may make them especially appealing and compelling for those who struggle within, and with others, with feelings of intense anger, aggression, and hostility. Such a state of affairs is not uncommon for people who, in their early life development or in later life experiences, have suffered major trauma, neglect, or abuse. Such individuals, when they first use opioids, discover the extraordinary calming and soothing effects of these drugs on their intense anger and rage, and thus they become powerfully drawn or attached to them.

Whereas opioid-dependent people have much difficulty controlling their feelings, especially anger and rage, those who prefer or who are dependent on depressants generally have the opposite problem: Namely they are too controlled or too tightly wrapped around their feelings. As is the case with other substance abusers, developmental life experiences, in this case often involving distrust and traumatic disappointment, have had a special influence on their experience of emotions. People who prefer depressants have special difficulties experiencing emotions involving loving or caring feelings, interpersonal dependency, and closeness; in psychological terms, they are defensive and repressed around these emotions and have difficulty in experiencing or expressing them. Depressants (e.g., alcohol, Seconal, Xanax) have appeal for these people because such drugs help them to relax their defenses and release them from their repressions. Mainly, such drugs briefly (the short- or quick-acting depressants) produce a sense of safety and an inner sense of warmth, affection, or closeness that otherwise these people cannot experience or allow.

Finally, stimulants (i.e., amphetamines and cocaine are the most popular and widely used) have appeal for those who suffer with overt and/or subtle states of depression, mania, and hyperactivity, in which problems with activation, activity, and energy are common. For example, ambitious driven types, for whom performance, prowess, and achievement are essential, find such drugs especially appealing on two counts: (1) stimulants are uplifting when individuals become depressed as their goals and ambitions, often unrealistic, fail them; (2) stimulants are facilitating and make action and activity easier when such people are on the upswing, making it easier for them to be the way they like to be when they are performing at their best. Stimulants cast a wide net of appeal because they also counter feelings of low energy, low activity, and low self-esteem in those suffering with overt or less overt (unrecognized or atypical) depression. Finally, those individuals suffering with attention deficit-hyperactivity disorder (ADHD), often sub-clinical or not recognized, are also drawn to and become dependent on stimulants because of the paradoxically opposite calming effect that stimulants have for people with this disorder—much like hyperactive children who are calmed by the prescribed stimulant Ritalin.

SELF-REGULATION VULNERABILITIES

To explain why people become addicted, early psychodynamic theory places great emphasis on subconscious and unconscious factors, pleasure and aggressive instincts or drives, and the symbolic meaning of drugs. To some extent, the stereotype of substance abusers as pleasure-seeking destructive characters (to self and others), in part, persists and derives from these early formulations. Albeit useful and innovative at the time, much of this early perspective is perceived in the early twenty-first century as outdated, counterempathic, and a disservice to understanding the motives of addicted and alcoholic individuals.

In contrast, the self-medication hypothesis has evolved from contemporary psychodynamic theory, which has placed the centrality of feelings (or affects) ahead of drives or instincts and has emphasized the importance of self-regulation, involving self-development or self-esteem (i.e., self-psychology), relationship with others (i.e., object-relations theory), and self-care (i.e., ego or structural psychology/theory). These contemporary psychodynamic findings have evolved since the 1950s, based on the works of investigators such as Weider and Kaplan; Milkman and Frosch; Wurmser, Krystal, Woody and associates; Blatt and associates; and Wilson, Dodes, Burton, Director, and Khantzian.

Although the self-medication hypothesis has gained acceptance as an explanation for drug/

alcohol dependency, it is not without its critics and it fails to deal with at least two fundamental problems or observations. First, many individuals suffer with the painful feelings and emotions that substance abusers experience, but they do not become addicted or alcoholic. Second, the self-medication hypothesis fails to take into account that addicted and alcoholic individuals suffer as much if not more as a result of their drug/alcohol use, and this point might appear to contradict the hypothesis that substances are used to relieve suffering.

Many of these criticisms, inconsistencies, and apparent contradictions are better understood or resolved when addictive problems are considered more broadly, in terms of self-regulation vulnerabilities or as a self-regulation disorder. For humans, life is the constant challenge of self-regulation, as opposed to the release, relief, or control of instincts and drives as early theory suggested. What is in need of regulation involves feelings, the sense of self (or self-esteem), relationships with others, and behavior. Those prone to addictive problems are predisposed to be so because they suffer with a range of self-regulation vulnerabilities. Their sense of self, including self-regard, is often shaky or defective from the outset of their lives. A basic sense of well-being and a capacity for self-comfort and self-soothing is very often lacking or underdeveloped from the earliest phases of development. Subsequent development of self-esteem and self-love, if it develops at all, remains shaky and inconsistent, given the compromised sense of self from which self-regard evolves. Needless to say, a poor sense of self or low self-esteem (which usually originates in a compromised or deficient self-other parenting relationship), ultimately affects subsequent self-other relationships and profoundly affects one's capacity to trust or to be dependent upon or to become involved with others. Psychodynamic formulations suggest that the self-regulation problems of addicted individuals are experienced as feelings of helplessness and powerlessness and play out in omnipotent posturing and dissociation.

It should not be surprising, then, that for some the energizing and activating properties of stimulants help self-doubting reticent individuals to overcome their depressive slumps and withdrawal, or that the soothing, relaxing effects of depressants help individuals who are restricted and cut off from others to break through their inhibitions and briefly experience the warmth and comfort of human contact that they otherwise do not allow or trust or that those whose lives are racked by anger and related agitation would find a drug such as heroin (an opioid analgesic) to be a powerful containing, calming antidote to their intense and threatening emotions, which disrupt them from within and threaten most of their relationships with others. These examples, and those previously covered in relation to self-medication motives that govern drug use and dependency, help demonstrate the how and why of specific drug effects, which often become so compelling that they may consume the lives of some users.

The regulation of feelings (or affects) and self-care are among the most compelling self-regulatory problems; they combine to make dependence on substances more likely than any other self-regulation factors. Focus on these two factors explains clearly why most people who suffer subjective painful emotions do not necessarily become addicted as well as why so many substance abusers persist in using debilitating substances despite the great suffering that ensues from their abuse.

The psychoanalytic perspective assumes that substance abusers suffer in the extreme with their emotions: They feel too much or they feel too little. When there is too much, drugs can relieve the intense unbearable feelings that addicts and others experience. Where there is too little and people are (or seem to be) devoid of, cut off from, or confused by their feelings (e.g., alexithymia, disaffected, or affect deficits), addicts prefer to counter the helplessness and loss of control caused by their lack of feelings. They choose to use drugs to change and control their feelings, even if doing so causes them more distress. They exchange feelings that are vague, confusing, and out-of-control, for drug-induced feelings that they recognize, understand, and control, even if such are painful and uncomfortable. Therefore, the factors of relief and control dominate people's motives for depending on drugs, even if these people have to endure the pain that their dependence on drugs also entails.

Finally, deficits in self-care (again deriving from early-life developmental problems) make it likely that certain individuals will become involved with hazardous activities and relationships that lead to drug experimentation, use, and dependence. Self-care

deficits refer to a major self-regulation problem, wherein individuals feel and think differently in potential or actually dangerous situations and activities, including those that involve drug/alcohol experimentation and use. Where most people would be apprehensive or frightened or would anticipate some guilt and shame, addictive and alcoholic-prone individuals show little or no such worry. Studying these patients' pre- and post-addictive behavior patterns often reveals similar unfeeling, unthinking, fearless behavior in conducting other aspects of their lives; for example, preventable accidents, health-care problems, and financial difficulties seem evident and common. Being out of touch with, or not feeling, their feelings (that is, their affect deficits or disaffected state) contributes to their self-care problems and thus makes it more likely that they would engage in the dangerous pursuit of drug/alcohol abuse, whereas others with better self-care functions would not (even in those instances in which the unbearable psychological suffering and states of distress are like those experienced by addicts). In this respect, painful or unbearable feelings, alone, are not sufficient to cause substance abuse or dependence. Rather, it is when individuals lack adequate self-care capacities and experience intense suffering that conditions exist for addictive behavior to develop or be likely.

See also **Conduct Disorder and Drug Use; Families and Drug Use; Religion and Drug Use.**

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RACE/ETHNICITY

There is a common perception that minority groups in the United States, particularly African Americans and Hispanics, use drugs more than Caucasians, even though population epidemiologic data show little difference in drug use among these groups. In fact, minority groups are, overall, less likely to use licit or illicit drugs. However, according to a 2003 report by the National Institute on Drug Abuse, the adverse consequences of substance abuse tend to be greater for minorities than for Caucasians.

The percentage of minority groups in the U.S. population is projected to increase rapidly over the early decades of the twenty-first century. Therefore, it is important to monitor trends and reduce substance abuse–related disparities that adversely affect minority populations. Different patterns of use and addiction across races and ethnicities provide insights into how underlying risk and protective factors affect

substance use, addiction, and adverse consequences because race and ethnicity are markers of differences in these underlying factors. In addition, new knowledge regarding human genomic and neurobiological differences may help reduce disparities in substance use and addiction. Because racial and ethnic disparities widen with the consequences of substance use and addiction, research is needed to understand societal and interpersonal mechanisms that exacerbate such disparities.

RACE DIFFERENCES IN THE GENERAL POPULATION

Recent reports of the annual National Survey on Drug Use and Health (NSDUH; formally the National Household Survey on Drug Abuse [NHSDA]) support previous research in suggesting that Native Americans and Alaska Natives (NA/AN) suffer disproportionately from substance use and addiction compared with other racial groups in the United States. The 2002–2005 surveys show that NA/AN were significantly more likely to have past-year alcohol or illicit drug use disorders. In addition, the use of a variety of illicit drugs and cigarette smoking are considerably higher in this group compared to other racial groups. In contrast, the prevalence of substance use disorders among Asians and Pacific Islanders (APIs), as a whole, has generally been lower than in other racial/ethnic groups. Non-Hispanic African Americans tended to report lower rates of both alcohol and tobacco use than non-Hispanic Caucasians, although the prevalence of licit and illicit substance use disorders has become somewhat higher than in non-Hispanic Caucasians.

ETHNIC DIFFERENCES IN THE GENERAL POPULATION

Prevalence rates of substance use and addiction vary markedly across Hispanic subgroups. Compared to the general U.S. population, Puerto Ricans and Mexicans tend to have higher rates of licit and illicit substance use, problem alcohol use, and alcohol use disorders. In comparison, Cubans and Central Americans tend to have lower prevalence rates of these behaviors and disorders. Although prevalences of both licit and illicit substance use for APIs combined are generally lower than for any other racial groups, Native Hawaiians report higher levels of such substance use (both recent and lifetime). Their patterns of substance use and abuse are closer to Native Americans than Asian subgroups. As in Hispanic subgroups, prevalence rates of substance use and abuse are considerably different across Asian subgroups and appear to be changing over time. In the 1990s, rates among Japanese were highest. In the early 2000s, however, other subgroups, such as Koreans and Filipinos (and sometimes Vietnamese), appear to have higher use and abuse rates across several illicit drugs, alcohol, and tobacco. The immigration history of the ethnic groups and individuals are correlated with a variety of substance use and abuse indicators.

YOUTH PATTERNS

Data from the Monitoring the Future Study (MTF) and the Youth Risk Behavior Surveillance System (YRBSS) show remarkably consistent patterns indicating that African-American adolescents are less likely to use most illicit drugs, alcohol, and tobacco than their non-Hispanic Caucasian and Hispanic counterparts. Furthermore, the proportion of early-onset users is lower among African Americans than among non-Hispanic Caucasians and Hispanics. These patterns have been persistent over many years. Other school-based studies also support the finding that being African American is protective for a variety of substance use and abuse indicators during adolescence. However, data from adult populations show that the prevalence differences are smaller. In some instances, as in the 2002 NSDUH, rates of some illicit drugs, heavy alcohol use, and recent cigarette use among African Americans surpass those of Caucasians in the same age group. Longitudinal studies suggest that this narrowing of differences between African Americans and Caucasians reflect higher ratios of African American than Caucasian youth who continue to use substances once initiated, rather than reflecting cohort differences.

PATTERNS AMONG MIXED-RACE ADULTS AND YOUTH

With the 2000 Census's introduction of multiple race/ethnicity reporting, more information is available to document substance use and addiction patterns of people who self-identify with two or more races or ethnicities. The 2000-2003 NSDUH data show that the prevalence rates of past-month nicotine dependence, past-year alcohol dependence, and past-year illicit drug dependence were all highest among those who reported more than one racial heritage, compared to any monoracial groups.

Within each racial group, higher rates of use and abuse of most substances were documented among those who reported mixed heritage compared to those reporting only one race or ethnicity. This trend is most striking among adolescents. Being a mixed heritage adolescent was found to be a predictor of substance use and misuse independent of other sociodemographic and acculturation measures among Hispanics, African Americans, and APIs.

PSYCHIATRIC COMORBIDITY

Psychiatric disorders have long been known to co-occur with substance use problems and disorders. Very large surveys using diagnostic instruments have made it easier to examine a variety of psychiatric disorders at racial group, and sometimes ethnic group, levels. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) allowed detailed examination of both Axis I and II (personality) disorders, including those diagnoses with low prevalence estimates. Having a psychiatric disorder most frequently increases the odds of having a substance use disorder by a minimum of 50 percent, regardless of racial/ethnic category. However, the odds ratios exceeded 5.0 (reflecting a five-fold risk) for some racial groups for certain psychiatric conditions, even when adjusting for sex, age, income, marital status, education, religion, and urbanicity. A study using the NESARC data reported odds ratios of 7.7 and 5.6 for any past-year drug use disorder with any mood disorder and personality disorder, respectively, among Native Americans; 6.3 for any drug use disorder with any personality disorder among Hispanics; and 5.0 for any past-year alcohol use disorder with any personality disorder among Asians. Higher risk for comorbidity, therefore, is not necessarily a function of how pervasive a substance use disorder is within a specific racial or ethnic group. Future studies are needed to uncover the underlying mechanisms of excess comorbidity in different racial/ethnic groups.

TREATMENT AND EMERGENCY ROOM USE

The Treatment Episode Data Set (TEDS) provides information on the demographic and substance abuse characteristics of people admitted to substance abuse treatment. In 2005, TEDS reported approximately 1.8 million admissions to treatment for abuse of alcohol and drugs in facilities that report to individual state administrative data systems. Five substances accounted for 95 percent of all TEDS admissions in 2004: alcohol (39%), opiates (17%), marijuana/hashish (16%), cocaine (14%), and stimulants (9%). Among all racial/ethnic groups except Hispanics of Puerto Rican origin, primary alcohol use was the most frequently reported substance at treatment admission. However, the proportion reporting use of the next four most common substances (opiates, marijuana, cocaine, and stimulants) varied considerably by racial/ethnic group. Compared to the demographic distributions of all admissions, African Americans were more than twice as likely to be admitted for smoked cocaine abuse (52%) as all groups were (22%). Mexicans and APIs were over two times more likely to be admitted for methamphetamine abuse than was true for all groups.

Racial and ethnic variations are also shown in the Drug Abuse Warning Network (DAWN), which reports trends in drug-related emergency department visits and deaths. There are, however, missing race and ethnicity data in DAWN (i.e., the data were not tabulated or are unknown for about 15%). Nonetheless, some observed trends are consistent with TEDS data: reports of cocaine-related episodes are disproportionately higher in African Americans, and heroin-related episodes are higher in Hispanics.

General population surveys make it possible to assess undermet needs, assuming diagnostic criteria accurately capture treatment needs. For example, only about 15 percent of individuals who meet lifetime criteria for an alcohol use disorder report ever having received alcohol treatment. In addition, considerable racial differences exist in the receipt of treatment, among individuals meeting criteria for a substance use disorder. In the 2000–2002 NHSDA/NSDUH surveys, 7.2 percent of Asians, 11.0 percent of African Americans, and 10.1 percent of Hispanics who met past-year *DSM-IV* alcohol dependence criteria reported treatment in the past year. These rates are lower than the 14.7 percent of Caucasians who met the same criteria. Similar trends are observed for drug abuse treatment, except that 23.8 percent of African Americans who met *DSM-IV* drug dependence criteria reported treatment compared to 18.3 percent of Caucasians who met the same criteria. Overall, these surveys found that although African

Americans were more visible in treatment and emergency room facilities, Asian substance abusers represented a less visible segment of racial minority abusers.

OTHER ADVERSE CONSEQUENCES OF SUBSTANCE USE AND ADDICTION

Greater disparities for adverse consequences of substance abuse are evident in racial and ethnic minority communities. For example, disparities exist in reported rates of arrest, sentencing, and incarceration (in particular among African Americans); victimization; school dropout; and HIV/AIDS infection. Given the magnitude of these disparities, there is an urgent need to better understand the factors—such as socioeconomic status, discrimination, culture, neighborhood and environmental conditions, access to health care, and employment status—that place minorities at risk (or that may be protective) for substance use and its adverse consequences.

See also **African Americans, Ethnic and Cultural Factors Relevant to Treatment for; Chinese Americans, Alcohol and Drug Use among; Drug Abuse Warning Network (DAWN); Hispanic Americans, Alcohol and Drug Use among; Jews and Alcohol; National Survey on Drug Use and Health (NSDUH); Structured Clinical Interview for DSM-IV (SCID).**

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RUMI KATO PRICE

SENSATION SEEKING AND IMPULSIVITY

Sensation seeking is a multidimensional personality construct characterized as "the seeking of varied, novel, complex, and intense sensations and experiences, and the willingness to take physical, social, legal, and financial risks for the sake of such experience" (Zuckerman, 1979). Sensation seeking is often assessed using the Sensation Seeking Scale, containing 40 items divided into four subscales: Thrill and Adventure Seeking, Experience Seeking, Disinhibition, and Boredom Susceptibility. The four subscales are summed to produce an overall score. Drug users rate higher in sensation seeking than users of alcohol, revealing their willingness to take the extra risks associated with the use of illegal substances. Impulsive Sensation Seeking is a scale that combines sensation-seeking items with those of a closely related trait, impulsiveness (Zuckerman, 1993). Although distinct, these components overlap because they are inherently related to achieving an optimal level of stimulation and arousal. They may involve risk-taking behaviors such as driving while intoxicated, unsafe sexual behaviors, and criminal activities, all of which have elements of disinhibitory behavior, as well as thrill seeking. Novelty seeking is a highly correlated component of sensation seeking (Cloninger et al., 1993; Zuckerman & Cloninger, 1996).

Sensation seeking has been used as a criterion to classify alcoholics. Type II (Cloninger et al., 1981) and Type B (Babor et al., 1992) alcoholics are characterized by early age of onset of alcoholism, a positive family history of alcoholism, high sensation seeking, impulsive temperament, and greater severity of alcohol dependence. This paradigm has been extended to illicit substance use as well (Feingold et al., 1996; Ball et al., 1995). Type II/B alcoholism is found predominantly in men (Cloninger, 1987) and, in part, that may be because men score higher on sensation seeking scales than woman and they endorse its subscales differently than women (Zuckerman et al., 1978; Scourfield et al., 1996; Ball et al., 1984). However, sensation seeking has shown stronger associations with substance abuse in females than in men and can distinguish women who are pure substance abusers from those with comorbid anxiety (Scourfield et al., 1996).

Younger individuals score higher on sensation seeking than older individuals and have a concomitant tendency to discount the risks involved in drug use (Romer & Hennessy, 2007; Wills et al., 1998). Age, sensation seeking, and negative affectivity predict frequent risk-taking and substance use in young people (Desrichard & Denarie, 2005). Both sensation seeking and impulsivity are strongly associated with early age of onset of drinking (Dom et al., 2006) and with greater quantity and frequency of alcohol consumption and greater illicit drug use (Zuckerman, 1994). Adults in treatment who score high on sensation seeking generally have an earlier age of onset of both alcohol consumption and alcohol abuse (Ball et al., 1994). High sensation seeking was significantly associated with methamphetamine and stimulant use in 17,000 young adults participating in the 2002 National Survey on Drug Use and Health (NSDUH) (Herman-Stahl et al., 2007). Sensation seeking has been associated with the use of club drugs (Low & Gendaszek, 2002), but possibly with frequency of use rather than initiation of use (Simons et al., 2005).

The biological basis for the association between sensation seeking and a vulnerability to substance abuse has been sought for many years. Low platelet monoamine oxidase (MAO) has long been associated with risk-taking behaviors (Buchsbaum et al., 1976; Fowler et al., 1980). Decreased MAO activity results in an increase in dopamine (as well as other monoamine neurotransmitters, including norepinephrine and serotonin). The increased dopamine drives reward-seeking structures in the striatum and nucleus accumbens in the brain resulting in an increased use of alcohol and drugs. A positive feedback loop results because alcohol and drugs cause a further increase in the release of dopamine in the

ventral striatum and nucleus accumbens. However, the relationship of low platelet MAO to personality factors such as sensation seeking is not understood as of 2008. Platelet MAO might be correlated with brain MAO-B and affect the rate of monoamine degradation: It may influence the level of a trace amine that itself is related to behavior; it might be correlated with other mitochondrial enzymes and reduce the functioning of an entire neurotransmitter system; or it might be a marker of expression of a set of monoamine neurotransmitter genes (Oreland et al., 2004). The evidence suggests that platelet MAO is a genetic marker of alterations in several neurotransmitter systems. This evidence stems from the fact that no genetic polymorphisms have been identified in MAO-B (Pivac et al., 2006) and complete inhibition of MAO-B does not change behavior in knock-out mice (Holschneider et al., 2001), or in humans after administration of MAO-B inhibitors in Parkinson's patients (Oreland et al., 2004). Platelet MAO levels correlate to CSF 5-HIAA levels, which have also been found to be higher in type II alcoholics (Virkkunen & Linnoila, 1993), suggesting involvement of the serotonergic system. If sensation seeking is linked to the reward centers in the brain, then norepinephrine levels should differ by sensation seeking level. Sensation seeking was strongly associated with both testosterone and norepinephrine in 74 healthy male adults (Gerra et al., 1999). In summary, neurobiological evidence shows that monoaminergic (dopaminergic, noradrenergic, and serotonergic) neurotransmitter systems play an important role in impulsivity.

Sensation seeking is estimated to be 48 percent to 63 percent heritable (Koopmans et al., 1995; Benjamin et al., 1996). Alleles of genes encoding the D1, D2, and D4 dopamine receptors and the dopamine transporter have been associated with sensation seeking.

See also **Adolescents and Drug Use; Conduct Disorder and Drug Use; Impulsivity and Addiction; Prevention.**

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CHERYL BESELER

SEXUAL AND PHYSICAL ABUSE

There has been considerable variation in the estimated prevalence of childhood sexual abuse (CSA), with estimates from early studies ranging from 6 to 60 percent in females and from 3 to 30 percent in males (Fergusson & Mullen, 1999). At least some of this variation may be attributed to variations in the definition of CSA itself, with some studies confining the definition to incidents involving rape or attempted rape and others utilizing broader definitions, including noncontact forms of sexual abuse. Child maltreatment or physical abuse is also relatively common: A recent study of 15,197 young adults in the United States estimated that 28.4 percent of the population experienced physical assault as a child, 11.8 percent experienced physical neglect, and 41.5 percent reported being left at home as a child, which was interpreted as being indicative of supervisory neglect (Hussey, Chang, & Kotch, 2006). Nevertheless, considerable controversy remains concerning the

definition of child maltreatment and the extent to which retrospective reports of these events are reliable and valid.

In general, there have been two principal approaches to studying factors associated with child maltreatment. The first of these relies on an examination of individuals identified through official records (e.g., police or treatment agency records) as having a known history of exposure to child maltreatment. Although this approach provides valuable insights, it is limited in its ability to provide an accurate appraisal of the consequences of child maltreatment, as those identified through official records may be unrepresentative of all individuals exposed to child maltreatment (typical estimates suggest that only a fraction of individuals who experience child maltreatment ever come to official attention). A second approach relies on retrospective assessments of childhood experiences in general population samples of adults. Although this approach has the potential advantage of identifying a representative sample of individuals exposed to childhood maltreatment, increasing concerns exist about the reliability and validity of retrospective reports of childhood abuse because individuals may either forget, decline to report, or, more controversially, repress memories of abuse. Indeed, follow-up studies have suggested that a substantial proportion of individuals with known histories of childhood maltreatment may not report such histories during an interview (Widom & Morris, 1997; Widom & Shepard, 1996).

Fergusson and colleagues (2000) examined the reliability of retrospective reports of child maltreatment within the context of a repeated measures design, in which individuals were evaluated twice. They reported relatively low consistency in reports of CSA and regular physical punishment: Approximately half of those reporting such behaviors at age 18 did not report them at the other assessment. These inconsistencies in reports lead to an underestimation of the prevalence of abuse. For example, the application of latent class analysis estimated the prevalence of CSA as 30.4 percent in females and 6.1 percent in males (relative to estimates based on single reports of between 13.9–17.3% among females and 2.7% among males). However, although there was considerable instability in abuse reports, further analyses indicated that errors in reporting were largely unrelated to outcome risks and did not influence estimated associations between childhood abuse and adult psychopathology (including alcohol and illicit drug abuse or dependence).

EXPOSURE TO CHILDHOOD SEXUAL ABUSE AND LATER ADJUSTMENT

Although both childhood sexual and physical abuse are remarkably common, considerable controversy surrounds the extent to which exposure to child abuse may have deleterious effects on subsequent well-being, including possibly increasing risks for alcohol and other drug use, abuse, and dependence. In addition to concerns about the representativeness of samples identified through official records and the reliability and validity of retrospective reports described above, early work in this area was plagued by a number of further methodological weaknesses, including small and nonrepresentative samples, and inadequate control for potentially confounding covariates that could act to increase both the risks of experiencing abuse and, independently of this, the risks for subsequent psychopathology.

One early study that addressed many of these methodological weaknesses was reported by Fergusson and colleagues (1996), who examined associations between the extent of exposure to CSA (no abuse, noncontact, contact, rape or attempted rape) and a range of psychiatric and substance use outcomes after control for a range of factors, including socioeconomic status, family disruption, childhood adversity, parenting practices, and parental criminal offenses and illicit drug use, which were associated with increased risks of CSA. Sample members had been studied from birth and thus prospective assessments of these risk factors were available, although self-reports of CSA were not assessed until age 18. Results indicated that CSA involving intercourse or attempted intercourse was associated with a 2.7-fold increase in the odds of alcohol abuse and a 6.6-fold increase in the odds of other substance abuse or dependence. Importantly, evidence of a strong dose-response relationship between the extent of CSA and risks of alcohol and drug abuse or dependence existed.

Although research on the longer-term sequelae of other forms of child maltreatment is plagued

by many of the same methodological issues as research on CSA, an emerging consensus is that childhood physical abuse increases the risk for subsequent alcohol and other drug use disorders, that a dose-response association exists between the extent of physical abuse and later outcomes, and that these associations are independent from the effects of social, family, and contextual factors which may be associated with increased risks for experiencing physical abuse during childhood. For example, Hamburger and coworkers (2008) reported that school students who reported experiencing physical abuse were over twice as likely to report early onset alcohol use, whereas Fergusson and Lynskey (1997) found that severe physical punishment or maltreatment was associated with elevated rates of alcohol abuse or dependence in young adulthood.

In addition to studies employing general population samples and attempting to control for background differences between individuals exposed and not exposed to maltreatment, there is also an emerging literature based on genetically informative research designs that have attempted to address the issue of whether maltreatment, and specifically CSA, make independent contributions to the risks for substance use disorders in adulthood. For example, in a sample of female twins discordant for CSA, Kendler and colleagues (2000) reported that CSA was associated with a 2.83-fold increase in the odds of alcohol dependence. Although an elevated risk of other drug dependence is present in those exposed to CSA, relative to their nonexposed co-twin, this association did not reach statistical significance, likely due to the relatively low number of discordant twin pairs and the low base rate of other drug dependence in this general population sample. Dinwiddie et al. (2000) reported that CSA was associated with a marginally significant elevation in the odds of alcohol dependence in women (OR = 2.50, 95% CI = 0.97–6.44) but not in men, although the nonsignificant association in males may partly be a function of reduced statistical power, as Dinwiddie and coworkers were able to identify only 25 male twin pairs who were discordant for exposure to CSA. Similarly, Nelson et al. (2002) identified twin pairs discordant for CSA from a larger sample of Australian twins and reported that those individuals who reported experiencing CSA had significantly elevated rates of both alcohol and nicotine dependence compared to their own co-twin who had not experienced CSA. In a follow-up to this study using the same sample of twins discordant for CSA, Nelson and colleagues (2006) reported that CSA was also associated with elevated rates of cannabis and other illicit drug abuse or dependence.

GENE BY ENVIRONMENT INTERACTIONS

Given the emerging consensus that childhood maltreatment is strongly associated with alcohol- and other drug-related problems (as well as with a range of other psychiatric and related conditions), increasing attention is focusing on the mechanisms underlying these putatively causal associations. There is increasing interest in—and evidence for—the role of gene by environment (GxE) interactions in the development of psychopathology (Rutter, Moffitt, & Caspi, 2006). Jaffee and colleagues (2005) found that childhood physical maltreatment was associated with dramatically elevated risks for the development of conduct disorder in those with a genetic vulnerability to this disorder, whereas in those without such a genetic predisposition, physical maltreatment was associated with only a very modest increase in risks of conduct disorder. Similarly, Caspi and his colleagues demonstrated significant interactions between childhood abuse—and other measures of childhood disadvantage or stress—and functional polymorphisms in two different genes (one that encodes the enzyme monoamine oxidase A [MAO-A], and the other that encodes the serotonin transporter protein) on outcomes frequently correlated or comorbid with alcohol and drug dependence, including antisocial behavior (Caspi et al., 2002) and depression (Caspi et al., 2003). Kaufman and coworkers (2007) found interactive effects of childhood maltreatment and the functional genetic polymorphism in the serotonin transporter gene on the onset of drinking and heavy drinking in childhood. A GxE interaction was also seen among sexual abuse survivors involving the MAO-A gene, alcoholism, and antisocial personality disorder (Ducci et al., 2008).

IMPLICATIONS FOR PREVENTION

Although childhood abuse is associated with increased risks for the development of alcohol- and other drug-abuse dependence (as well as other

psychiatric disorders), it is not the case that maltreatment inevitably leads to maladjustment, with some studies suggesting that approximately 30 to 40 percent of individuals who experience child maltreatment will not meet diagnostic criteria for any psychiatric disorder. For example, in a follow-up to the Isle of Wight studies, Collishaw and colleagues (2007) reported that 44.5 percent of those reporting childhood abuse did not meet criteria for any Axis I psychiatric disorder. Factors associated with resilience included perceived parental care, adolescent peer relationships, adult relationships, and personality.

Consideration of official reports of child victimization suggests that rates of physical and sexual abuse of children may have declined in the United States in the early twenty-first century: Specifically, Jones and colleagues (2006) reported that substantiated cases of physical abuse declined by 36 percent and substantiated case of CSA by 47 percent during the 1990s. While acknowledging potential limitations in official reports of child maltreatment, Jones and colleagues argue that at least some component of this observed change may reflect a real decline in cases of child maltreatment which they attribute to a number of possible causes, including direct prevention efforts, economic improvements, more aggressive criminal justice efforts, improved and increased use of psychiatric medications, and generational changes. There appeared, however, to be no corresponding decline in cases of child neglect. Nonetheless, the analysis by Jones and colleagues (2006) suggests promise for a reduction in—or even elimination of—child maltreatment. Given convincing evidence of long-term adverse consequences associated with exposure to child maltreatment, it is clear that a promising avenue for the reduction of alcohol and other drug problems (as well as other psychopathology) would involve efforts to reduce further the occurrence of childhood sexual and physical abuse. This effort could be coupled with treatment and interventions that have increasingly been shown to be effective in ameliorating the adverse effects of exposure to childhood maltreatment (Cohen, 2005; MacDonald et al., 2006).

See also **Child Abuse and Drugs; Childhood Behavior and Later Substance Use; Families and Drug Use; Intimate Partner Violence and Alcohol/Substance Use.**

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MICHAEL T. LYNSKEY

STRESS

The term *stress* refers to processes involving perception, appraisal, and response to harmful, threatening, or challenging events or stimuli (Levine, 2005; Sinha, 2005). Stressful experiences can be emotionally or physiologically challenging and can activate stress responses and adaptive processes to regain homeostasis (Charmandari et al., 2005; McEwen, 2007). Examples of emotional stressors include interpersonal conflict, loss of relationship, and death of a close family member or loss of a child. Common physiological stressors are hunger or food deprivation, sleep deprivation or insomnia, psychoactive drug use, and extreme increases or decreases in body temperature. The differences between emotional and physiological stressors allow for separate consideration of (1) internal and external events or stimuli that exert demands or load on the organism; (2) the neural processes that evaluate the demands and assess availability of adaptive resources to cope with the demands (appraisal); (3) the subjective, behavioral, and physiological activity that signal stress to the organism; and (4) behavioral, cognitive, and physiological adaptation to the stressful event.

While stress is associated with negative affect and distress, it has been linked with positive effects too. For example, "good" stress includes external and internal stimuli that are challenging and increase arousal, but limited in duration, resulting in cognitive and behavioral responses that generate a sense of mastery and accomplishment, and can be perceived as pleasant and exciting (Levine, 2005; McEwen, 2007). Such situations rely on adequate motivational and executive functioning to achieve goal-directed outcomes and homeostasis (Levine, 2005; Paulus, 2007; McEwen, 2007). However, the more prolonged, repeated, or chronic the stress—that is, states associated with increased intensity or persistence of distress—the greater the uncontrollability and unpredictability of the stressful situation, the less the sense of mastery or adaptability that results and the greater the magnitude of the stress response and risk for persistent homeostatic dysregulation (Meaney et al., 2002; McEwen, 2007). Thus, the dimensions of intensity, controllability, predictability, mastery, and adaptability are important in understanding the role of stress in increasing the risk of maladaptive behaviors such as addiction.

The perception and appraisal of stress rely on specific aspects of the presenting external or internal stimuli, personality traits, availability of internal resources, and prior emotional state, including beliefs and expectancies. Specific brain regions mediate the appraisal of stimuli as distressing and the resulting physiological, behavioral and emotional experiences and adaptive responses. Brain regions such as the amygdala, hippocampus, insula, orbitofrontal cortex,

and medial prefrontal and cingulate cortices are involved in the perception and appraisal of emotional and stressful stimuli; the brainstem (locus ceruleus and related arousal regions), hypothalamus, thalamus, and striatal and limbic regions are involved in the physiological and emotional responses to stress. Together these regions contribute to the experience of distress. The physiological responses are manifested through the two major stress pathways: (1) the hypothalamic-pituitary-adrenal (HPA) axis, in which corticotrophin releasing factor (CRF) is released from the paraventricular neucleus (PVN) of the hypothalamus, which stimulates adrenocorticotrophin hormone release from the anterior pituitary and subsequently stimulates the secretion of cortisol/corticosterone from the adrenal glands, and (2) the autonomic nervous system, which is coordinated via the sympathoadrenal medullary (SAM) systems (Phan et al., 2005; Charmandari et al., 2005).

In addition, extrahypothalamic CRF in the corticostriatal limbic pathways has an extensive influence in modulating subjective and behavioral stress responses (Heinrichs, 2005). Central catecholamines, particularly noradrenaline and dopamine, are involved in modulating brain motivational pathways (including the ventral tegmental area (VTA), nucleus accumbens (NAcc), and the medial prefrontal (mPFC) regions) that are important in regulating distress, exerting cognitive and behavioral control and negotiating behavioral and cognitive responses critical for adaptation and homeostasis (Phan et al., 2005). The hypothalamic and extrahypothalamic CRF pathways and central catecholamines target brain motivational pathways to critically affect adaptive and homeostatic processes. For example, different parts of the medial prefrontal cortex are involved in higher cognitive or executive control functions, such as controlling and inhibiting impulses, regulating distress, focusing and shifting attention, monitoring behavior, linking behaviors and consequences over time, and considering alternatives before acting and decision-making responses (Roberts et al., 1998). Psychosocial and behavioral scientists have elegantly shown that with increasing levels of emotional and physiological stress or negative affect, there is a decrease in behavioral control and an increase in impulsivity, such that increasing levels of distress and persistence of stress increase the risk of maladaptive behaviors (Mischel, 1996; Tice et al., 2001; Hayaki et al., 2005; Greco & Carli, 2006; Fishbein et al., 2006; Verdejo-García et al., 2007; Anestis et al., 2007; Hatzinger et al., 2007). From neurobiological studies, increasing stress has been shown to decrease prefrontal functioning and increased limbic-striatal level responding, which perpetuates low behavioral and cognitive control (Sinha, 2005; Li & Sinha, 2008). Thus, the motivational brain pathways are key targets of brain stress chemicals and provide a potential mechanism by which stress affects addiction vulnerability and relapse risk.

STRESS AND INCREASED RISK OF ADDICTION

Considerable evidence from population-based and clinical studies supports a positive association between psychosocial adversity, negative affect and chronic distress, and addiction vulnerability. Adolescents facing high recent negative life events show increased levels of drug use and abuse (Sinha, 2005). Longitudinal studies support the effects of stress on drug use initiation and escalation in adolescents and young adults (see review in Sinha, 2005; Wills et al., 2006).

Overwhelming evidence exists for an increased association between childhood sexual and physical abuse and victimization and increased drug use and abuse (Sinha, 2005). In addition to sexual and physical abuse, negative affect and chronic distress states—such as mood and anxiety disorders, including post-traumatic stress disorder (PTSD)—and behavioral conduct problems are predictive of addiction vulnerability (Brady & Sinha, 2005; Cichetti & Toth, 2005). Findings indicate that negative affect, including temperamental negative emotionality, are associated with substance abuse risk (Measelle et al., 2006). Furthermore, there are sex differences in the effects of early trauma and maltreatment on the increased risk of addiction (MacMillan et al., 2001; Simpson & Miller, 2002; Hyman et al., 2006).

Evidence also indicates that lifetime exposure to stressors and cumulative adversity has a significant impact on addiction vulnerability after accounting for a number of control factors such as race/ethnicity, gender, socioeconomic status, prior drug abuse, prevalence of psychiatric disorders, family history of substance use, and behavioral and conduct problems (Turner & Lloyd, 2003; Lloyd & Turner, 2008). Findings indicate that cumulative instances of stressful events are predictive of alcohol and drug dependence in a dose-dependent manner, after accounting

for control factors. The dose-dependent effects of cumulative stressors on risk for addiction exist for both genders and for Caucasian, African American and Hispanic race/ethnic groups. The types of adverse events significantly associated with addiction vulnerability are parental divorce or conflict; abandonment; being forced to live apart from one's parents; loss of a child by death or removal; unfaithfulness of a significant other; loss of one's home to natural disaster; death of a loved one; emotional abuse or neglect; sexual abuse; rape; physical abuse by a parent, caretaker, family member, spouse or significant other; being a victim of a shooting or other violent act; and observing violent victimization. These represent highly stressful and emotionally distressing events, with uncontrollable and unpredictable stress characteristics.

All of the above findings indicate the need to examine evidence supporting the possible mechanisms that explain how stress increases addiction vulnerability. Animal and human studies indicate that the reinforcing properties of drugs of abuse are mediated by the mesolimbic dopaminergic (DA) pathways, which include dopamine neurons originating in the ventral tegmental area and extending to the ventral striatum (nucleus accumbens) and the prefrontal cortex (Pierce & Kumaresan, 2006; Volkow et al., 2007 Oswald et al., 2005). This pathway is also involved in assigning salience to stimuli, in reward processing, and in learning and adaptation (Kauer & Malenka, 2007).

Furthermore, stress exposure and increased levels of glucocorticoids (GC) also enhance dopamine release in the NAcc (Sinha, 2005; Pruessner et al., 2004; Oswald et al., 2005), and drug-induced increases in cortisol are associated with both dopamine binding in the ventral striatum and with ratings of amphetamine-induced euphoria (Wand et al., 2007). Suppression of GC by adrenalectomy reduces extracellular levels of dopamine under basal conditions and in responses to stress and psychostimulants, and chronic GC inhibits DA synthesis and turnover in the NAcc (Pacak et al., 2002; Sinha, 2005). These data suggest that DA transmission is highly sensitive to alterations in the HPA axis and glucocorticoid secretion. Furthermore, drugs of abuse, stress, and concomitant increases in CRF and glucocorticoids are known to enhance glutamate activity in the VTA, which in turn enhances activity of dopaminergic neurons (Saal et al., 2003; Wang et al., 2005).

Finally, stress-related alterations in the mesolimbic DA pathways could impact additional regions connected to DA pathways, such as the amygdala, hippocampus, insula, and related corticolimbic regions, which are involved in reward, learning, and adaptive and goal-directed behaviors (Everitt & Robbins, 2005; Kauer & Malenka, 2007). These regions, along with the mesolimbic DA pathways, play an important role in interoception, emotion and stress processing, impulse control and decision making, processes that promote loss of control, compulsions, and addictive processes that increase the risk of developing addiction (Baler & Volkow, 2006; Li & Sinha, 2008).

CHRONIC DRUG USE AND VULNERABILITY TO STRESS

Acute, regular, and chronic use of the most commonly abused drugs such as alcohol, nicotine, cocaine, amphetamines, and marijuana that activate brain reward pathways (mesocorticolimbic dopaminergic systems) have direct effects on brain stress pathways (Koob & Kreek, 2007; Chen et al., 2008). Chronic use of drugs also alters stress responses in addicted individuals compared to healthy volunteers, with addicted individuals showing greater emotional and behavioral distress and stress and cue-induced craving and blunted stress hormone responses compared to healthy volunteers (Al'Absi et al., 2005; Fox et al., 2007; Sinha et al., 2008). Regular and chronic use of drugs of abuse and acute withdrawal states are also associated with a downregulation of the mesolimbic dopamine pathways, and decreases in basal and stimulated dopamine have been reported in several preclinical studies (Nader et al., 2006; Koob et al., 2004; Mateo et al., 2005) and in human brain imaging studies (see review by Volkow et al., 2007). Chronic cocaine use also dramatically alters central noradrenergic pathways in the ventral and dorsal striatum, other areas of the forebrain, and the ventromedial prefrontal cortex (Beveridge et al., 2005; Porrino et al., 2007). Thus, there are significant physiological, neurochemical, and behavioral alterations in stress and dopaminergic pathways associated with chronic drug use, and these changes are accompanied by enhanced sensitivity to distress and drug craving when addicts

are faced with environmental stress or drug-related stimuli known to increase drug craving and drug use.

Although there are efficacious treatments to address alcoholism and drug abuse, rates of relapse remain high for these disorders (Sinha, 2007). Research in humans has also begun to assess whether early life and/or chronic stress and psychobiological markers of stress and craving states contribute to the high rate of relapse outcomes in alcohol and drug use disorders. Childhood trauma and psychiatric distress have been associated with treatment outcome and relapse rates, with some evidence of sex differences in the extent of the association (Brady & Sinha, 2005; Hyman et al., 2008). Among cocaine dependent individuals, stress-induced cocaine craving in the laboratory significantly predicted time to cocaine relapse. While stress-induced ACTH and cortisol responses were not associated with time to relapse, these responses were predictive of the amount of cocaine consumed during follow-up (Sinha et al., 2006). Although in this study drug cue-induced craving was not predictive of relapse, there was a high correlation between stress and cue-induced drug craving and in stress and cue-induced HPA responses.

There is also evidence that stress responsivity has an impact on relapse outcomes in alcohol and nicotine dependence. Negative mood and stress-induced alcohol craving and blunted stress and cue-induced cortisol responses have been associated with alcohol relapse outcomes (see Sinha, 2007 for review). Nicotine-deprived smokers exposed to a series of stressors show blunted ACTH, cortisol and blood pressure responses to stress but increased nicotine withdrawal and craving scores, and these responses were predictive of nicotine relapse outcomes (Al'Absi et al., 2005). Thus, for alcoholic and smoking samples, as in those with cocaine dependence, it appears that the drug craving state marked by increasing distress and compulsive motivation for the drug (craving), along with poor stress regulatory responses, results in an enhanced susceptibility to addiction relapse. These data support the need for addressing stress-related changes in the treatment of addiction in order to decrease the high rates of relapse observed in substance abuse.

Clearly, stress and adaptation are related to addictive behavior. Facing stress is basic to all organisms, but how people adapt to stress can differ significantly across individuals. The close interaction between stress neurobiology and susceptibility to drug use, abuse, and relapse are important areas of research. Acute and chronic stress and life adversity may increase the risk of developing substance abuse. Drugs of abuse affect the stress pathways, and the interaction between stress and reward/motivational circuits are vital for participating in adaptive, goal directed behaviors. Growing evidence suggests that the effects of chronic stress and drug abuse interact to increase both the risk of developing and of perpetuating substance abuse. Future advances in the understanding of these interactions is expected to lead to specific prevention and treatment efforts to decrease the stress-related vulnerability to risk of substance abuse.

See also **Addiction: Concepts and Definitions; Endorphins; Epidemiology of Drug Abuse; Families and Drug Use; Intimate Partner Violence and Alcohol/Substance Use.**

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ROCKEFELLER DRUG LAWS. The Rockefeller drug laws are a set of New York mandatory sentencing statutes for drug crimes. They were proposed by New York's Governor Nelson A. Rockefeller in reaction to a heroin epidemic in his state. These laws, which took effect on September 1, 1973, require that judges impose lengthy prison sentences on drug traffickers, with a large category of drug offenders receiving life imprisonment. The goal was to deter people from both drug use and trafficking by imposing tough and certain punishments. Although the law was immediately challenged as violating the Cruel and Unusual Punishment clause of the U.S. and New York constitutions, the New York Court of Appeals unanimously upheld the law

Within a few years, however, the state's prison population began to swell as increasing numbers of defendants were subjected to the provisions of the Rockefeller laws. From 1969 to 1979, the prison population doubled from 12,000 to 24,000. In the same time period, the percentage of incarcerated nonviolent drug offenders increased from 10 percent to over 30 percent. In spite of these laws, the crime rate continued to grow. A major evaluation concluded that neither drug use nor drug trafficking was reduced after the law was passed. The likelihood that a defendant, once arrested, would be incarcerated did not increase—although the likelihood that a defendant, once convicted, would be imprisoned did increase (Joint Committee on New York Drug Law Evaluation, 1977).

The processing of cases became much more expensive for New York. For every crime affected by the law, the percentage of defendants pleading guilty fell and the proportion of trials increased. The evaluators concluded that it "took between ten and fifteen times as much court time to dispose of a case by trial as by plea." The average time to handle a drug prosecution in New York City, for example, doubled, rising from 172 days in 1973 to 351 days in 1976.

Although the legislature realized the ineffectiveness of the stated purposes of the laws, neither it nor a succession of governors has proposed repealing the laws. Instead, the legislature has sought to amend the laws in ways that reduce their scope. In 1977, the legislature removed marijuana from the definition of crimes dealing with controlled substances and created a new sentencing law for marijuana sale and possession. The possibility of life imprisonment for marijuana offenses was eliminated.

The legislature tinkered with the laws again in 1979. This time it increased the amount of weight of the drug necessary to trigger higher-level felonies. It also reduced the minimum sentence range for certain drug convictions and eliminated a classification from the statute. The 1979 amendments also gave the courts the ability to retroactively resentence defendants who had been convicted based on the original weight and classification schemes.

Despite these changes, they have done little to reduce the harshness of the sentencing practices or reduce the prison population. In 2007, the state prisons held over 63,000 inmates. Twenty-two percent of the prison population is comprised of nonviolent drug offenders.

By the late 1990s, many in the legal community argued for repeal of the Rockefeller laws, believing that they imposed disproportionate punishment on nonviolent drug offenders and ignored drug treatment options. However, Governor George Pataki responded in 1999 with only a minor change in the laws. Pataki proposed legislation that would slightly alter the laws by offering first-time drug couriers a chance to cut their sentences by five years. Under this proposal, the appellate courts would be allowed to review and reduce sentences by five years for first-time felony offenders under the harshest provision of the laws, which now calls for a maximum of fifteen years to life. This proposal was similar to one proposed by Chief Judge Judith S. Kaye, who also called for allowing trial judges to defer the prosecution of nonviolent drug offenders for up to two years and to divert them to drug treatment programs. However, the legislature did not act on these reform efforts.

In 2004 the New York State legislature passed the Drug Law Reform Act (DLRA). Some of these reforms include lowered drug sentences, expanded eligibility for prison-based drug treatment, and the ability to apply for re-sentencing.

See also **Drug Laws, Prosecution of.**

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ROHYPNOL. Known by a variety of street names such as roofies, roach, R-2, trip and fall, and rope or "the date-rape drug," Rohypnol is the trade name for benzodiazepine flunitrazepam, a sedative-hypnotic drug used medically in a number of countries. Rohypnol has recently become a widely abused drug in Sweden, Mexico, Italy, the United Kingdom, the United States, and South Africa, a trend made more troubling by the fact that many users regard it as relatively safe. Rohypnol, in fact, has many dangerous and undesirable effects for the illicit user. It has been associated with an increased risk of violence and accidents as well as stupor, coma, memory loss, and death. Its ability to induce unconsciousness and amnesia has led to its use in sexual assaults in the United States (hence, its reputation as a date-rape drug) as well as robberies.

Although never approved for use in the United States (where it is illegal) Rohypnol is a commonly prescribed benzodiazepine in Europe and elsewhere. Like other benzodiazepines, such as Valium (Diazepam) or Xanax (Alprazolam), it is useful in the medical treatment of sleep disorders and anxiety, though only under supervision by a doctor. Benzodiazepines act at brain receptors for the inhibitory neurotransmitter GABA, which is also the site of action for another, older class of sedative-hypnotic drugs and barbiturates. Although generally safer than barbiturates, benzodiazepines like Rohypnol share some of the same dangers, especially when mixed with ethanol, a common practice among

Rohypnol tablets. DAVID HOFFMAN PHOTO LIBRARY/ALAMY.

illicit drug users. These dangerous effects range from incontinence, behavioral disinhibition, violence, delirium, and blackouts to stupor, respiratory depression, and death. These effects all stem from the ability of rohypnol to depress brain function.

At lower doses, benzodiazepines can reduce anxiety and cause relaxation and a loosening of inhibitions somewhat similar to the effects of alcohol, another drug that acts as a depressant on the central nervous system. As with many abused drugs, the continued use of Rohypnol results in increased tolerance, requiring larger doses to produce the same effects. Larger doses mean narrower margins of safety and the increased incidence of side effects, especially memory loss and deficits in learning. Drinking alcohol in combination with Rohypnol makes serious consequences all the more likely. Of still greater concern for the illicit user is that chronic use of sedative-hypnotic drugs like Rohypnol can produce a level of physiologic dependence greater than that resulting from opiate drugs like heroin or morphine. Abrupt withdrawal from regular use can produce complications ranging from the relatively mild, such as restlessness and anxiety, to more severe effects like tremor, hallucinations and convulsions similar to those experienced during severe alcohol withdrawal. These complications can be best avoided through a medically supervised withdrawal.

Rohypnol has received much media attention in the United States for its apparent involvement in a number of sexual assaults or rapes. Because it can quickly render an unsuspecting victim unconscious, Rohypnol lends itself to this kind of crime. As Rohypnol is odorless and tasteless and easily dissolved in drinks, it can be offered to a victim without arousing suspicion. Although media attention has focused on particular drugs like Rohypnol and GHB, it should be noted that a variety of drugs can and are being used in this manner, including barbiturates, opiates, other benzodiazepines, and ethanol. Ethanol remains several times more likely to be associated with sexual assault than any other drug, including Rohypnol, even though Rohypnol and drugs like it are more effective in rapidly producing the stupor and memory loss desired by this type of criminal.

See also **Benzodiazepines; Gamma-Aminobutyric Acid (GABA); Neurotransmitters.**

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RUBBING ALCOHOL. Rubbing alcohol is known as isopropyl alcohol (C_3H_8O); it is one of the more useful of the commercial alcohols, included in hand lotions and many cosmetic items as well as in antifreeze or deicer products. A 70 percent solution of isopropyl alcohol has more germicidal properties than does ethanol (drinking alcohol), so it is used in many health-care situations, both in households and in medical facilities. It is also used for massages and by athletic trainers to treat skin and muscle groups, hence the term *rubbing*. It has a drying effect on the skin and causes blood vessels to dilate; its distinctive odor is associated with doctor's offices, since it is used to clean the skin being prepared for an injection.

When rubbing alcohol is ingested either pure or added to beverages, the result is toxic—with symptoms lasting longer than those seen after drinking ethanol (alcoholic beverages), because isopropyl alcohol is slowly metabolized to acetone, another toxic substance.

See also **Inhalants.**

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SCOTT E. LUKAS

Encyclopedia of Drugs, Alcohol & Addictive Behavior

Third Edition

HENRY R. KRANZLER & PAMELA KORSMEYER

ENCYCLOPEDIA OF

DRUGS, ALCOHOL & ADDICTIVE BEHAVIOR

THIRD EDITION

Volume 4

S–Z; Index

Pamela Korsmeyer and Henry R. Kranzler

EDITORS IN CHIEF

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SADD. *See* **Students Against Destructive Decisions (SADD).**

SCANDINAVIAN COUNTRIES. *See* **Nordic Countries (Denmark, Finland, Iceland, Norway, and Sweden).**

SCHIZOPHRENIA. Schizophrenia is a psychiatric illness that can be profoundly disabling and is usually chronic in nature. The cause is not known, but there appears to be a genetic predisposition. The etiology has been conceptualized in a stress/diathesis (vulnerability) model: Biological and environmental factors (e.g., drug abuse, psychosocial stresses) interact with a genetic vulnerability to precipitate the illness. Several theories have been proposed to explain the observed biological abnormalities of the disorder, including overactivity of the dopamine neurotransmitter systems in the central nervous system, changes in brain structure (e.g., enlargement of the lateral cerebral ventricles) and brain function (e.g., decreased frontal lobe function [hypofrontality], as evidenced by diminished blood flow, and deficits in attention and sensory filtering). Psychological and social factors are considered important in the expression and course of the disorder. It is likely that schizophrenia constitutes a group of disorders rather than a single entity; these disorders present with similar clinical signs and symptoms, but the etiologies, treatment responsiveness, and course of illness in each vary.

Detailed descriptions of the illness date back to the nineteenth century. Emil Kraepelin (1856–1926) used the term *dementia praecox* to describe psychiatric states with an early onset and deteriorating course. Eugen Bleuler (1857–1939) coined the term *schizophrenia* for a "splitting of the mind," in his belief that the illness was a result of the disharmony of psychological functions. The diagnosis of schizophrenia requires observation and clinical interviewing. No sign or symptom is specific for the illness, nor do any laboratory tests exist to establish the diagnosis. The *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (2000) contains the diagnostic guidelines of the American Psychiatric Association for schizophrenia. These include the presence of characteristic psychotic symptoms (delusions, hallucinations, a thought disorder, inappropriate emotion); impaired ability to work, social functioning, and self-care; and continuous signs of the illness for at least six months. The symptoms of an affected individual can change with time, therefore longitudinal follow-up is important. It should be noted that certain of these symptoms can be indicative of other conditions (including drug abuse [cocaine, crack, PCB, amphetamines], head injury, brain tumors, as well as other psychiatric disorders). Furthermore, it is important to take into account the educational level, intellectual ability, and cultural affiliation of the individual when making a diagnosis. The onset of illness is usually in late adolescence or early adulthood and is generally insidious. The typical course of schizophrenia is characterized

by exacerbations and remissions. A gradual deterioration in functioning generally occurs that eventually reaches a plateau. However, a small proportion of persons may recover. It is estimated that 20 percent to 30 percent of affected individuals can lead somewhat normal lives whereas another 20 to 30 percent continue to experience moderate symptoms.

The prevalence rates of schizophrenia vary to a limited degree worldwide, but in the United States the lifetime prevalence is estimated to be between 0.5 and 1.5 percent (about one in 50 to one in 150 people). In industrialized countries, there is a disproportionate number of schizophrenic patients in the lower socioeconomic classes. Some experts think this is due to the schizophrenic's loss of education and social opportunity, while others maintain this is more a direct result of the stresses of poverty.

The management of affected individuals involves hospitalization when there is an exacerbation of the illness, plus the use of medication. The mainstay of pharmacologic treatment is the class of drugs known as antipsychotics. Many antipsychotics are available and they act to control the psychotic symptoms; most of them do so by blocking the actions of the neurotransmitter dopamine. About 75 percent of patients respond to these drugs; however, there are side effects, including muscle stiffness, tremors, and weight gain. The drugs may also cause tardive dyskinesia (TD), a disorder that causes involuntary repetitive movements of the body, mouth, and tongue.

Some of the more commonly prescribed antipsychotics include: chlorpromazine, fluphenazine, haloperidol, olanzapine, and risperidone. The atypical antipsychotic clozapine has been identified as the best choice for managing resistant schizophrenia; however, up to 73 percent of patients treated with clozapine report clinically relevant side effects. These can be quite severe, and include potentially fatal neuroleptic malignant syndrome (NMS), myocarditis, cardiomyopathy, and dangerous lowering of the white blood cell count (for the latter, regular and frequent blood testing is required during the treatment period). In a study following 8,000 patients in Australia who started clozapine treatment between January 1993 and March 1999, fifteen developed myocarditis, and eight developed cardiomyopathy; a total of six patients died within the six years.

After a person has recovered from an acute episode of schizophrenia, the emphasis is on practical aspects of management: living arrangements, self-care, employment, and social relationships. Education of and support made available to family members are important and can have an impact on relapse rates in the patient. Many schizophrenic patients have to remain on antipsychotic medication for prolonged periods, since the rate of relapse is high after drug discontinuation. Side effects, primarily of a neurologic nature (e.g., TD), are a source of concern, but in most cases the benefits of symptom control outweigh the risks of pharmacotherapy. Making sure that the patient complies with medication use is often a problem.

See also **Amphetamine; Cannabis Sativa; Complications: Mental Disorders.**

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SCOPOLAMINE AND ATROPINE. Scopolamine (*d*-hyoscine) and atropine (*dl*-hyoscyamine) is a tropane alkaloid found in the leaves and seeds of several plant species of the family Solanaceae, including deadly nightshade (*Atropa belladonna*) and henbane (*Hyoscyamus niger*). Atropine, a major alkaloid in deadly nightshade, is also found in jimsonweed (*Datura stramonium*). In Europe, in centuries past, henbane was a component of socalled witches' brews or was applied as an ointment to mucous membranes. According to some folk tales, the idea that witches fly on broomsticks was derived from the sensation of a flying experience after the use of such ointments.

Scopolamine and atropine have very similar actions. They act as competitive antagonists at both peripheral and central muscarinic cholinergic receptors. Scopolamine is still sometimes used clinically for the treatment of motion sickness. The compound also causes central nervous system depression, leading to drowsiness, amnesia, and fatigue. It also has some euphoric effects and abuse liability, but these are not considered to be of such magnitude to require control of the drug under the Controlled Substances Act. Atropine has fewer actions on the central nervous system than scopolamine. It is used to reduce actions at peripheral cholinergic structures—it produces decreased gastric and intestinal secretions as well as spasms and also results in pupillary dilation. It blocks the action of the vagus nerve that results in slowing of the heart. It is often used before operations to prevent unwanted reflex slowing of the heartbeat.

High doses of either of these tropane alkaloids can cause confusion and delirium accompanied by decreased sweating, dry mouth, and dilated pupils.

See also **Alkaloids; Jimsonweed.**

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SECOBARBITAL. Secobarbital, prescribed and sold as Seconal, is a short-acting barbiturate used principally as a sedative-hypnotic drug but occasionally as a preanesthetic agent. It is a nonspecific central nervous system (CNS) depressant and greatly impairs the mental and/or physical abilities necessary for the safe operation of automobiles and complex machinery.

Before the introduction of the benzodiazepines, secobarbital was the drug most commonly used to treat insomnia. Prolonged or inappropriate use of secobarbital can produce tolerance and physical dependence. If high doses have been used, abrupt cessation can result in severe withdrawal symptoms that include convulsions. Secobarbital is more likely to be abused than benzodiazepines and appears to produce greater euphoria in certain individuals than would a comparable sedative dose of a benzodiazepine. Consequently, it is classified as a Schedule II class drug in the Controlled Substances Act, which indicates that although it is acceptable for clinical use, it is considered to have a high abuse potential. As with other barbiturates, secobarbital should never be combined with another CNS depressant because respiratory depression can occur.

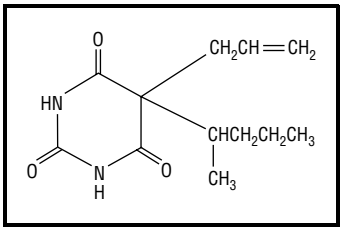

Figure 1. Chemical structure of secobarbital. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

See also **Abuse Liability of Drugs: Testing in Humans; Drug Interaction and the Brain; Drug Interactions and Alcohol.**

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SECULAR ORGANIZATIONS FOR SOBRIETY (SOS). Secular Organizations for Sobriety is a self-help organization for alcohol and drug users, founded as an alternative to Alcoholics Anonymous (AA) and other groups based on AA. It was intended to offer help to people who are uncomfortable with the emphasis on spirituality that is a central tenet of the AA Twelve-Step Programs. Founded by James Christopher, SOS began with a 1985 article. "Sobriety without Superstition," describing Christopher's own path to sobriety. SOS claimed in 1991 to have an international membership of 20,000, making it the largest of the alternative groups. In 1987, it was recognized by the State of California as an alternative to AA in sentencing offenders to mandatory participation in drug rehabilitation. Members of SOS are not necessarily nonreligious; however, many do not believe in an intervening higher power who takes responsibility for their individual problems.

Unlike AA—which emphasizes that the individual is powerless over alcoholism and must look to a "higher power" for help in achieving and maintaining sobriety—SOS and other alternative organizations assert the capacity of individuals to control their own behavior. SOS stresses total abstinence, personal responsibility, and self-reliance as the means to achieve and maintain sobriety (recovery), but the organization recognizes the importance of participating in a mutually supportive group as an adjunct to recovery. Members learn that open and honest communication aids in making the appropriate life choices that are essential to recovery. SOS shares with other self-help groups the importance of anonymity and the abstention from all drugs and alcohol.

SOS consists of a nonprofit network of autonomous nonprofessional local groups dedicated solely to helping individuals with alcohol and other drug addictions. It encourages and is supportive of continued scientific inquiry into the understanding of alcoholism and drug addiction.

Among other self-help organizations that see themselves as alternatives to AA are Rational Recovery (RR) and Women for Sobriety (WFS).

See also **Coerced Treatment for Substance Offenders; Models of Alcoholism and Drug Abuse; Treatment: An Overview; Treatment: An Overview of Alcohol Abuse/Dependence; Treatment: An Overview of Drug Abuse/Dependence.**

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SEDATIVE. Sedative is a general term used to describe a number of drugs that decrease activity, moderate excitement, and have a calming effect. The primary use for these drugs is to reduce anxiety, but higher doses will usually cause sleep (a drug used primarily to cause sleep is called a *hypnotic*). Although the term *sedative* is still used, the drugs usually prescribed to produce this calming effect are benzodiazepines, which are more commonly known as antianxiety agents or minor tranquilizers.

See also **Barbiturates; Drug Types; Sedative-Hypnotic.**

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SEDATIVE-HYPNOTIC. Sedative-hypnotic drugs are used to reduce motor activity and promote relaxation, drowsiness, and sleep. The term is hyphenated because by adjusting the dose, the same group of drugs can be used to produce mild sedation (calming, relaxation) or sleepiness. Thus the distinction between a sedative and a hypnotic (sleeping pill) is often a matter of

dose—lower doses act as sedatives and higher doses promote sleep.

In some people, sedative-hypnotics can produce a paradoxical state of excitement and confusion. This response tends to occur more frequently in the very young and older populations. Some of these drugs have the potential to be abused. Very high doses of most sedative-hypnotic drugs will produce general anesthesia and can depress respiration so much that breathing must be maintained artificially or death will occur. The benzodiazepines are an exception to this general rule in that higher doses typically produce sleep and are far less likely to severely depress respiration.

One of the first agents to be added to the list of the classic sedatives (alcohol and opiates) was bromide, introduced in 1857 as a treatment for epilepsy. Chloral hydrate was introduced in 1869 and paraldehyde was first used in 1882. The barbiturates were introduced in the early 1900s and remained the dominant drugs for inducing sleep and sedation until the bezodiazepines were developed in the late 1950s and early 1960s. A number of miscellaneous non-barbiturate sedatives (ethchlorvynol, glutethimide, carbromal, methylparafynol, methyprylon, methaqualone) were introduced in the 1940s and 1950s, and for a brief period rivaled the barbiturates in popularity, but their used declined rapidly along with the use of barbiturates. The bromides were recognized to have toxic properties, but they were still in use until the mid-twentieth century; chloral hydrate and paraldehyde were used well into the late 1970s and are still used in some places. Some drugs with other medical uses are prescribed as hypnotics, but the effectiveness of these substances remains to be proven in well-controlled clinical trials.

An advance in the development of sedative-hypnotics occurred with the discovery of non-benzodiazepine drugs that also act on the bensodiazepine receptor. Zolpidem and zaleplon are short-acting hypnotics that demonstrate fewer side-effects and less tendency for rebound insomnia when they are discontinued, a common problem with the benzodiazepines. These drugs also demonstrate less abuse potential than many of the other sedative-hypnotics and little respiratory depression.

See also **Abuse Liability of Drugs: Testing in Humans; Drug Interactions and Alcohol; Drug Types; Suicide and Substance Abuse.**

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SEDATIVES: ADVERSE CONSEQUENCES OF CHRONIC USE. Sedative drugs are also called hypnotics or sedative-hypnotics. They are sometimes referred to as minor tranquilizers or anxiolytics (antianxiety medications). Technically, a *sedative* decreases activity and has a calming effect whereas a *hypnotic* produces drowsiness, allowing for the onset and maintenance of sleep. Ideally, a hypnotic produces a state of sleep similar to natural sleep and from which the sleeper may be easily awakened. The same drug used for sedation, pharmacologically induced sleep, and general systemic anesthesia may be seen to induce a continuum of central nervous system (CNS) depression. Such drugs are usually referred to, therefore, as sedative-hypnotics, and they are widely prescribed in the treatment of insomnia (sleep problems). Although some people take these drugs only occasionally and for specific sleep problems (e.g., secondary to grief, time-limited stress, long-distance flights), many more take them over prolonged periods (months, and even years) as a presumed aid to nightly sleep. They do this despite medical advice that restricts the use of such drugs to approximately two weeks.

All the sedatives are available in tablets or capsules for oral dosage, and some are also available for intravenous or intramuscular administration.

Almost all sedatives have the same behavioral effects as alcohol (ethanol). Many individuals who abuse sedatives, are, or have been, problem drinkers. According to guidelines published by the American Psychiatric Association (1990), patients with a history of alcoholism or other drug abuse problems should not be treated with benzodiazepine sedatives on a chronic basis because they are at a high risk of developing benzodiazepine abuse. This, however, remains a controversial issue (Ciraulo & Nace, 2000).

USE OF HYPNOTICS

Sleep problems in adults are of three main types:

1. Problems of falling asleep (sleep initiation);
2. Problems staying asleep (sleep maintenance);
3. Early-morning wakening.

Sleep-onset problems vary little with age; early-morning wakening is often secondary to depression, and sleep-maintenance problems show a clear and marked increase with aging. Whereas approximately 10 percent of young adults complain of serious sleep problems, this increases to 30 to 50 percent of those aged 70 or older (Morgan, 1990). This age-related pattern for complaints of insomnia is reflected in the pattern of use of sedative-hypnotic drugs. The results of one survey indicate that 4 percent of people older than 65 used a hypnotic agent continuously for more than a decade (Morgan et al., 1988). According to a 2002 poll conducted by the National Sleep Foundation, 15 percent of the subjects polled reported using a sleep aid (either prescription or over-the-counter) at least a few nights per month. Across all age groups, roughly twice as many women as men take sedative-hypnotic drugs.

COMMONLY USED HYPNOTICS

The most commonly prescribed hypnotics include the benzodiazepines temazepam (Restoril) and triazolam (Halcion). Some sedative benzodiazepines are also used to induce sleep including alprazolam (Xanax), lorazepam (Ativan), and diazepam (Valium). Newer agents include the non-benzodiazepines zolpidem (Ambien), zaleplon (Sonata), and eszopiclone (Lunesta). Although these drugs differ chemically from the benzodiazepines, their mode of action is similar in that they target the same receptors in the brain. The newest sedative, ramelteon (Rozerem), is a melatonin agonist. It differs both chemically and pharmacologically from the benzodiazepines. Other, older hypnotics are chloral hydrate (Noctec), a chloral derivative, and hydroxyzine (Vistaril), an antihistamine.

BENZODIAZEPINES

Although the use of benzodiazepines as sedative-hypnotic drugs is decreasing in favor of newer agents, they are still prescribed with great frequency. The key concerns in the use of the benzodiazepines as a hypnotic are:

1. Adverse effects experienced while the patient is taking the drug;
2. Possible physical and psychological dependence;
3. Rebound insomnia and withdrawal symptoms when the patient stops taking the drug.

Classification. Benzodiazepines can be classified on pharmacokinetic grounds into three groups: long-acting (e.g., flurazepam [Dalmane], diazepam, chlordiazepoxide [Librium]), medium-acting (temazepam), and short-acting (triazolam, oxazepam [Serax], lorazepam) sedative-hypnotics. Their efficacy, at least in short-term use, has been well documented. The pattern of improvement in sleep corresponds fairly closely with the pharmacokinetic properties of each drug, providing that factors of absorption and elimination are taken into account. For example, temazepam is absorbed relatively slowly and has little effect on sleep-initiation time whereas triazolam is absorbed relatively rapidly, which brings sleep on more quickly.

Each sedative-hypnotic has a minimally effective dose but the dose that is usually effective may be twice as high as the minimum. Further increases may, however, cause side effects and rebound insomnia without substantially improving sleep. In sleep-laboratory studies many benzodiazepines lose their efficacy after about two weeks of nightly use. Subjectively, however, patients often feel that their sleep is improved for longer periods than this.

Adverse Effects. Benzodiazepine sedatives have three major adverse effects:

1. Cumulative effects with repeated dosage, particularly if the patient has not yet metabolized the previous dose;

2. Additive effects when given with other classes of sedatives or with alcohol;
3. Residual effects after the medication is discontinued.

Patients taking benzodiazepines may feel drowsy, have reduced psychomotor speed, and impaired concentration. These in turn can adversely affect their ability to function, so they should be cautioned about driving and operating machinery while taking these drugs. The longer-acting the drug, the more pronounced these effects. Tolerance to these sedative effects builds up to some extent with repeated use of the drug.

All benzodiazepines can impair the user's ability to learn and remember new information. This memory impairment is most pronounced a few hours after taking the drug, so when taken as a sleep aid such effects may be much reduced by the time the person wakes the next morning. As with other adverse effects, higher doses cause greater problems. Rarer adverse effects include disinhibition and aggressive behavior. These effects have been reported for some benzodiazepines (e.g., triazolam, flunitrazepam [Rohypnol, not marketed in the United States]) more than others.

Rebound insomnia refers to the heightened insomnia that may occur when the patient stops taking the drug, such that the sleep pattern is actually worse than it was before the medication. Studies have established that rebound insomnia is generally at its worst following the use of shorter-acting benzodiazepines and at its least following the use of longer-acting benzodiazepines (Roehrs et al., 1986). Rebound is clearly dose-related, and the patient should be prescribed the lowest effective dose, with rebound effects described to warn the patient about overdosing for faster or better drug-induced sleep.

Age-related changes in the way that drugs are metabolized and excreted mean that benzodiazepines accumulate more in older patients and, therefore, adverse effects are more pronounced in the elderly, who are particularly susceptible to the effects of these drugs on their psychomotor performance (e.g., balance and gait). Consequently, older patients taking benzodiazepine sedatives are especially at risk of falls resulting in hip or femur fractures and are at an increased risk of being involved in a motor vehicle accident. In elderly patients with cognitive deterioration or dementia, use of a benzodiazepine may intensify these symptoms.

Abuse, Dependence, and Withdrawal. Some argue that rebound insomnia is itself a sign of physiological dependence on benzodiazepine hypnotics (e.g., Morgan, 1990). Others insist that dependence is shown only when withdrawal from a drug leads to symptoms other than a rebound of the original problems. In general, psychological dependence on benzodiazepines can develop rather rapidly. After only a few weeks, patients who attempt to discontinue the medication may experience restlessness, disturbing dreams, paranoid ideas and delusions, and feelings of tension or anxiety in the early morning. Withdrawal following the use of a moderate dose of a benzodiazepine may include dizziness, increased sensitivity to light and sound, and muscle cramps. Abrupt withdrawal following high-dose usage may result in seizures and delirium.

The syndrome of withdrawal from benzodiazepines may be slow in onset because these drugs remain in the body for relatively long periods. Withdrawal appears to be most severe in patients who used benzodiazepines that are absorbed rapidly and have a rapid decline in blood serum levels (e.g., alprazolam, lorazepam, and triazolam). In patients who abuse both benzodiazepines and alcohol, a delayed benzodiazepine withdrawal syndrome may complicate withdrawal from alcohol. Patients who are high-dose abusers of benzodiazepines usually require inpatient detoxification.

Abuse. Animal studies indicate that benzodiazepines, like cocaine and opioids, activate a reward pathway in the brains of most mammals. In humans the benzodiazepines have reinforcing effects that appear to be more pronounced in frequent users of other recreational drugs. For example, alcoholics and heroin addicts will at times use benzodiazepines to extend the supply of their most-preferred drug because alcohol and heroin are also depressants.

Abuse of benzodiazepines by themselves is relatively unusual but sometimes occurs among users who seek a high from massive amounts of these drugs. Street drug dealers sell benzodiazepines at a relatively low cost in most major cities. Some abusers combine benzodiazepines with other drugs to enhance the effects; for example, some believe that taking diazepam half an hour after an oral dose of

methadone will produce a high that is more intense than can be obtained from taking either drug by itself.

Overdose. Benzodiazepine overdose is a serious though rarely fatal event unless accompanied by the concomitant ingestion of alcohol or other CNS depressants. Symptoms of benzodiazepine overdose include sleepiness, incoordination, and diminished mental facilities. In more serious cases, low blood pressure, respiratory depression, and coma can occur. In a conscious patient, treatment usually begins with the inducement of emesis (vomiting). In an unconscious patient, the contents of the stomach are removed by gastric lavage (stomach pumping). In addition to supportive care, a benzodiazepine antagonist, flumazenil (Romazicon) can be used to improve the level of consciousness.

NON-BENZODIAZEPINE HYPNOTICS

Newer compounds include such non-benzodiazepine hypnotics as eszopiclone (Lunesta), zolpidem (Ambien), and zaleplon (Sonata), which act either atypically or selectively on benzodiazepine receptors. They are also known as benzodiazepine receptor agonists though they are chemically distinct from benzodiazepines (and from each other). They are short-acting drugs and at normal clinical doses cause little residual sedation (hangover). The risk of rebound insomnia or dependence with these compounds is much lower than with benzodiazepines, but not absent (Lader, 1992). Memory problems have been reported with these agents. A phenomenon called *sleep driving* in which an individual operates a motor vehicle without memory of the event has been associated with zolpidem. Retrograde amnesia, a condition in which the patient cannot recall events immediately prior to taking the drug, has been reported in patients who have taken zalepon.

OTHER SEDATIVE/HYPNOTIC DRUGS

Barbiturates. Barbiturates were used until the 1950s as sleeping pills but were superseded by the benzodiazepines. With the exception of phenobarbital (Luminal), which is still used as a sedative and as an anticonvulsant, the barbiturates are rarely prescribed.

Chloral Derivatives. These compounds, which include chloral hydrate, are sometimes used with elderly patients because they are less likely to cause restlessness in confused or demented patients. Chloral derivatives are also relatively safe to give to children for sedation before or after surgery. They can, however, cause gastric irritation and rashes.

Antihistamines. Antihistamines, commonly used for the treatment of allergies, often cause drowsiness, leading to their use as sedatives. Diphenhydramine (Benadryl, Nytol, Sominex) and hydroxyzine (Atarax, Vistaril) are two antihistamines often prescribed for patients who need only a mild sedative. They are safe and do not produce dependency. They should not, however, be used together with alcohol. The most common side effect of these medications is dry mouth.

Buspirone. Buspirone (BuSpar) is the only anti-anxiety medication that is not a sedative. Because it does not produce depressant effects or dependence, it is used in the treatment of depression as well as anxiety. Unlike the sedatives, buspirone does not affect the patient's alertness or motor skills, it does not intensify the effects of alcohol, and it does not produce a withdrawal syndrome. Because it has no potential to be abused or to produce dependence in patients with a history of drug or alcohol dependence, buspirone may be the anxiolytic of choice for these patients.

Melatonin Agonists. Melatonin is a natural sleep-inducing hormone produced by the pineal gland in the brain. Natural melatonin has been used to induce sleep. Ramelteon, a prescription drug that works on melatonin receptors in the brain, is the most recently approved sedative and is believed to lack the potential to cause dependence or abuse.

See also **Accidents and Injuries from Drugs; Addiction: Concepts and Definitions; Aging, Drugs, and Alcohol; Barbiturates; Barbiturates: Complications; Benzodiazepines: Complications; Drug Interaction and the Brain; Drug Interactions and Alcohol; Memory, Effects of Drugs on.**

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SEIZURES OF DRUGS. The seizure of drugs in the United States is a salient consequence of a variety of enforcement programs, particularly interdiction programs. These seizures provide evidence that the U.S. criminal justice system is imposing a cost on individuals involved in drug distribution. A large seizure, in particular, offers the most vivid evidence that those at the upper echelon of the illicit drug trade are subject to serious risks.

Seizures from smugglers have often been used as a measure of the effectiveness of interdiction efforts. One argument suggests that the larger the quantity of drugs seized, the more smugglers have been hurt by interdiction. Others view seizures as an indicator of the quantity smuggled. This view assumes that the percentage of imports seized is effectively a constant. These are clearly extreme assumptions. In fact, the quantity seized is a function of at least three factors: (1) the quantity shipped, (2) the relative skill of the interdictors, and (3) the care taken by smugglers. The last element—which is generally given the least attention in discussions of seizures—probably depends on the replacement cost of the drugs. In other words, if that cost goes down (e.g., because of good growing conditions in the producer country), smugglers will invest less in the concealment and protection of shipments. As a result the seizure rate (i.e., the percentage of shipments seized) is likely to rise.

Seizures of cocaine rose throughout the 1980s, reflecting both the rapid increase in total shipments and the declining replacement cost of the drug. Between 1989 and 2003, annual federal cocaine seizures fluctuated around 250,000 pounds and only exceeded 300,000 pounds twice (1992 and 1994). In 2004 and 2005, federal seizures for cocaine exceeded 380,000 pounds each year, and they remained above 330,000 pounds in 2006. Marijuana seizures grew dramatically during the same period. Federal authorities seized about 1.1 million pounds in 1989, and by 2006 this figure had exceeded 2.5 million pounds. This was largely a result of increased cultivation and production of marijuana within the United States itself. Between 1989 and 1999, federal heroin seizures ranged between 1,700 and 3,500 pounds with no clear trend. There was a large jump in 2000 and in 2002 over 6,000 pounds of heroin were seized by federal officials. Federal heroin seizures declined

from 2002 to 2005, and there was a slight increase in 2006 to more than 3,900 pounds.

Methamphetamine seizures nearly doubled between 2002 and 2006, increasing from 5,500 pounds to over 10,000 in that time. Mexico is the main source of methamphetamine for the U.S. market, and many of these seizures occurred on the Southwest border. MDMA ("Ecstasy") seizures increased dramatically in the 1990s, with the Drug Enforcement Administration reporting that it seized less than 200 tablets in 1993 and more than 3 million tablets in 2000. This estimate is probably low, however, because the DEA is not the only federal agency that seizes drugs (the Federal Bureau of Investigation and U.S. Coast Guard also do so, for example).

Drugs are also seized by state and local enforcement agencies, but estimates are difficult to calculate at these levels. The growth of domestically grown marijuana has placed state and local police closer to the criminal activity. The number of domestic cannabis plants seized more than doubled between 2000 and 2007—from 2.8 million plants to 7 million plants, respectively. In addition, the proliferation of domestic methamphetamine labs made such facilities targets for federal, state, and local law enforcement agencies. Lab seizures increased from 6,777 in 1999 to over 10,000 in 2003, but they decreased dramatically between 2005 and 2007 (5,935 labs were seized in 2005; 4,002 were seized in 2006; and only 1,802 labs were seized from January to October 2007).

See also **Cocaine; Drug Interdiction; Heroin; International Drug Supply Systems; Marijuana (Cannabis); MDMA; Methamphetamine; Operation Intercept; U.S. Government: Agencies in Drug Law Enforcement and Supply Control; U.S Government Agencies: U.S. Customs and Border Protection (CBP).**

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See **SMART Recovery and Rational Recovery.**

SEMI-STRUCTURED ASSESSMENT FOR DRUG DEPENDENCE AND ALCOHOLISM (SSADDA).

The Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA) is a diagnostic instrument that was developed for studies of the genetics of substance use and psychiatric disorders. The SSADDA was based on the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA), a comprehensive psychiatric interview schedule developed for use in the Collaborative Study on the Genetics of Alcoholism (Bucholz et al., 1994).

The SSADDA was developed to provide detailed coverage of drug dependence and other DSM-IV diagnoses (American Psychiatric Association, 1994) that commonly co-occur with these disorders. It is available in a computer-assisted format that allows the interviewer to enter subjects' responses directly. The computerized format includes such features as automatic "skip-outs," a cross-checking function to identify inconsistent responses, a running tabulation of diagnostic criteria, and a check for out-of-range

values. These features streamline the interview process and aid in the collection of accurate information. The computerized SSADDA also permits direct uploading of data to a database. This eliminates the time-consuming steps of data entry and verification (with their potential for errors) and permits the ready generation of DSM-IV diagnoses using scoring algorithms.

The SSADDA allows a trained (non-clinician) interviewer to identify a variety of substance use and psychiatric disorders by collecting information about the onset of symptoms and about their severity and duration. The interview includes detailed questions about the onset of symptoms for the major drugs of abuse, including cocaine and opioids. In addition, the SSADDA contains sections covering attention deficit hyperactivity disorder and pathological gambling, which are theoretically and clinically relevant to substance dependence. Finally, the SSADDA includes a section on environmental factors, including adverse childhood experiences, which are considered likely to have an impact on the risk of drug and alcohol dependence.

A useful feature of the SSADDA that was retained from the SSAGA is the assessment of the relationship between alcohol and drug dependence clusters and the occurrence of other psychiatric disorders (Bucholz et al., 1994). The dates of occurrence of alcohol and drug use, clustering of problems, periods of abstinence from alcohol and drug use, and dates of psychiatric disorders are correlated. This makes it possible to categorize the respondent's history of psychiatric disorders as being either completely independent of substance problems or including at least some symptoms occurring in temporal association with substance use.

The SSADDA has been shown to yield reliable diagnoses for alcohol and drug dependence disorders, as well as a variety of psychiatric disorders (Pierucci-Lagha et al., 2005). The reliability for individual diagnostic items was also generally good, with minimal impact of any individual criterion on diagnostic reliability(Pierucci-Lagha et al., 2007). This is consistent with the idea that the DSM-IV diagnosis of substance dependence measures an underlying construct that is relatively consistent across specific substance categories. Although the SSADDA was developed for use in genetic studies, its broad and detailed coverage of disorders and its computer-assisted format allow it to be used in a variety of applications requiring careful diagnostic assessment.

See also **Diagnostic and Statistical Manual (DSM); Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA); Structured Clinical Interview for DSM-IV (SCID).**

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SEMI-STRUCTURED ASSESSMENT FOR THE GENETICS OF ALCOHOLISM (SSAGA).

The Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) is a research diagnostic interview designed to obtain a detailed psychiatric history of current and past mental health problems among adults, ages 18 and older (Bucholz et al., 1994). Developed by the Collaborative Study on the Genetics of Alcoholism (COGA) for use in its large-scale, multisite extended family study of the genetics of alcohol dependence, this research diagnostic interview covers the major Axis I psychiatric disorders defined in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised (DSM-III-R) and fourth edition (DSM-IV). The SSAGA also covers antisocial personality disorder (ASPD). Psychiatric diagnoses for many of the disorders covered can also be made using the Feighner,

DSM-III-R, and ICD-10 criteria sets. Special attention has been given to assessing comorbid psychiatric conditions, identifying the ages of onset and recency of different diagnoses, and distinguishing symptoms due to alcohol and drug use from symptoms typically seen in affective disorders or antisocial personality disorder.

In addition to the different diagnoses covered, the SSAGA contains sections that assess demographics, medical history, suicidality, and the home environment in which the person was raised. The SSAGA-II is an excellent instrument for assessing current and past psychiatric problems in clinical samples as well as in samples from the general population. Designed for use by lay interviewers, the SSAGA has been used in more than 200 studies in the United States and abroad and has been translated into nine foreign languages.

The Alcohol section of the SSAGA is comprehensive and was designed to assess alcohol use and the physical, psychological, social, and psychiatric manifestations of acute and chronic alcohol use in adults. The SSAGA differs from many other research diagnostic interviews in that it includes an assessment of alcohol abuse and dependence, the alcohol dependence syndrome, the alcohol withdrawal syndrome, the flushing response, periods of abstinence, and treatment history. This section also includes questions that are not used in diagnostic schemes but may be useful for characterizing alcohol use and problems (i.e., developing alcohol-related phenotypes that may be useful in studies of the genetics of alcoholism).

Considerable care has been taken to establish the reliability and validity of the SSAGA, which been shown to have good intra- and interrater reliability among raters from the COGA project trained to use it (Bucholz et al., 1994). A second study documented the reliability of the individual criterion items for psychoactive substance dependence and their impact on diagnosis (Bucholz et al., 1995). A third study compared the diagnoses of subjects interviewed twice: once by the SSAGA and again by the Schedule for Clinical Assessment in Neuropsychiatry (SCAN). The findings from the two interviews were highly similar, which supports the validity of the SSAGA (Hesselbrock et al., 1999).

The SSAGA is part of a suite of interviews developed by COGA for use in family studies. In addition to the SSAGA, COGA also developed companion instruments to assess children ages 6–12 (C-SSAGA-C), adolescents ages 13–17 (C-SSAGA-A), and parents regarding their children's mental health status (C-SSAGA-P). The reliability of the adolescent interview, the C-SSAGA-A was examined and confirmed by Kuperman et al. (2001). A separate Family History Assessment Module (FHAM; Rice et al., 1995) was designed to obtain psychiatric history information on unavailable or deceased family members. The FHAM first screens "classes" of relatives of family members for a history of mental health problems using the family history/family story method. Individuals who are suspected of having a history of mental health problems can then be queried using the Individual Assessment Module. Family history diagnoses can be made using *DSM-III-R* or *DSM-IV*.

See also **Diagnostic and Statistical Manual (DSM); Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA); Structured Clinical Interview for DSM-IV (SCID).**

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Each of these instruments is in the public domain. Copies of the versions of the SSAGA and associated documentation can be obtained at no charge via the Internet by accessing the Washington University (St. Louis, Mo.) COGA Web site at http://zork.wustl. edu/niaaa.

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VICTOR HESSELBROCK

SENSATION AND PERCEPTION AND EFFECTS OF DRUGS. Every behavior in which an organism engages involves information from the primary senses, such as vision, hearing (audition), and touch. A number of drugs of abuse alter sensory information. Mind-altering drugs can also influence perception of time, thinking, behavior, and mood. Often abusers of these drugs experience severe depression, anxiety, paranoia, confusion, and terror.

Naturally occurring drugs, such as mescaline from the peyote cactus, increase awareness of visual and auditory sensations and also produce visual illusions and hallucinations. The psilocybin mushroom (Mexican or magic mushroom) produces similar effects. Because of these sensory changes, mescaline and psilocybin have been used since pre-Columbian times in religious ceremonies by the peoples of Mexico and the American Southwest.

Lysergic acid diethylamide (LSD), an artificially produced drug that was first synthesized in the late 1930s by the Swiss chemist Albert Hoffmann, has become well known for producing intense and colorful visual sensations. People also report changes in sensory behavior with drugs that are related to LSD (such as DMT, DOM, and MDMA, also known as Ecstasy or the "love drug"). DMT is a short-acting (cycle takes less than one hour) crystalline powder that produces visual hallucinations. DOM, also known as STP, is more than 50 times as potent as mescaline. MDMA produces "out-of-body" sensations and acts as a stimulant. Phencyclidine (PCP) is another synthesized drug that is sometimes added to the list of drugs that alter sensory behavior; however, its sensory effects are limited to numbness in the hands and feet. Ketamine, also known as Special K, is a veterinary medicine that is chemically similar to PCP; its effects range from delirium to inability to move.

The active constituent of marijuana, tetrahydrocannabinol (THC), also produces alterations in sensory behavior; however, hallucinations—such as those produced by mescaline or LSD—are less common with THC, although there is an increased risk of psychotic symptoms among users with a family or personal history of psychosis. Cocaine and amphetamine sometimes produce hallucinations and other sensory distortions, but only when they are taken for long periods of time.

Various names are used to describe drugs that alter sensory behavior. One term is *psychedelic*, which refers to mind-expansion or to experiencing events that go beyond normal boundaries; this word was coined in 1956 by Humphrey Osmond, a British psychiatrist. Another term is *psychotomimetic*, which refers to the similarities of hallucinations that occur in psychotic disorders, such as schizophrenia, and those produced by mescaline and LSD. The term *hallucinogenic* is slightly misleading, since not all drugs that alter sensory behavior produce hallucinations.

OBSERVATIONS IN HUMAN SUBJECTS

Most of our information about drugs and the ways in which they alter sensory behavior in people comes from individual reports (called anecdotal) rather than from well-controlled laboratory studies. People have reported vivid images, changes in perception, and hallucinations after they have taken mescaline or LSD. Synesthesias—a mixing of the senses, such as "the hearing of colors" or "the seeing of sounds"—may also occur. One of the first descriptions of LSD's effects is recounted as follows:

> I was seized by a peculiar sensation. . . . Objects, as well as the shape of my associates in the laboratory, appeared to undergo optical changes. . . . With my eyes closed, fantastic pictures of extraordinary plasticity and intensive color seemed to surge toward me. After two hours this state gradually wore off (Julien 1988, p. 180).

Although these sensory disturbances stop within a few hours, some people experience confusion, sensory distortions, or poor concentration for longer periods of time. For some people, drug effects recur long after the drugs have left their systems—these brief episodes are called *flashbacks.*

STUDIES IN THE LABORATORY

Since alterations in sensory behavior, such as hallucinations, cannot be observed directly, it is very difficult to examine these effects in laboratory animals. One way to investigate a drug's effect on sensory behavior is to train animals to behave differently in the presence of different types of visual or auditory stimuli. If a drug changes the animal's behavior, it is possible that these changes in behavior are due to a change in how well the animal hears or sees the stimuli. Another type of procedure examines how intense (e.g., how loud or how bright) a stimulus has to be for an organism to hear or see it. In these procedures, the intensity required to hear or see a stimulus is determined before a drug is given and then it is compared to the intensity required to hear or see the stimulus after the drug is given.

In general, drugs such as mescaline, LSD, and THC do not alter an animal's ability to tell the difference between visual or auditory stimuli—nor do they alter visual or auditory thresholds. This lack of effect in animals suggests one of two explanations: either drugs such as LSD produce different effects in animals than they do in people, or, more likely, the procedures that are used to study alterations in sensory behavior in animals do not measure the unique ways in which drugs such as LSD alter sensory behavior.

Conversely, MDMA testing has found comparable results in both animals and humans. A late 1990s study (conducted on red squirrel monkeys) at Johns Hopkins University showed that MDMA has damaging effects on memory. Published in 2000, a British study of both current and previous MDMA users has discovered both immediate and delayed memory deficits.

See also **Inhalants; Opiates/Opioids; Research, Animal Model: An Overview.**

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LINDA DYKSTRA
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SEROTONIN. Chemically named 5-hydroxytryptamine (5-HT), serotonin is a monoamine transmitter found in neurons that project widely throughout the brain and spinal cord. The actions of 5-HT are mediated by at least fourteen genes that encode subtypes of 5-HT receptors (5-HTXR) that are as of 2008 grouped into seven families (5-HT1R – 5-HT7R) according to structural and functional characteristics. A ligand-gated ion channel (the 5-HT3R) and thirteen distinct receptors coupled to various effector systems influence the concentration within the neuron of ions such as K+ (potassium) and Ca+ (calcium) and thereby the activity of the cell. Permissive (5-HT1AR, 5-HT1BR, 5-HT2AR, 5-HT3R, 5-HT4R) and inhibitory (5-HT2CR) roles for 5-HT receptors localized within brain reward pathways appear to underlie 5-HT-elicited control over the abuse liability of several classes of abused drugs, including cannabinoids, ethanol, opiates, and psychostimulants (e.g., cocaine, nicotine). Cocaine, the best studied in this regard, results in the accumulation of 5-HT in the synapse consequent to reuptake inhibition, and this elevated synaptic 5-HT plays a fundamental and complex role in the processes that underlie the progression of cocaine addiction. Once the 5-HT1R and 5-HT2R

subtypes are distinguished pharmacologically from one another, an excitatory role for the 5-HT1BR and 5-HT2AR and an inhibitory role for the 5-HT1AR and 5-HT2CR are evident in the control of cocaine-induced behaviors. In particular, the 5-HT2AR and the 5-HT2CR are known to control the neurochemical and behavioral effects of cocaine. Preclinical studies indicate that 5-HT2AR antagonists and/or 5-HT2CR agonists may effectively reduce craving and/or relapse and, likewise, enhance abstinence, whereas 5-HT2CR agonists may also effectively reduce cocaine intake in active cocaine users. Thus, serotonergic systems present great promise in the quest to define susceptibility to the behavioral effects of abused drugs, addictive processes, and/or relapse after recovery, and open the door to the development of new medications for the management of abuse and addiction.

See also **Lysergic Acid Diethylamide (LSD) and Psychedelics; Monoamine; Neurotransmitters; Receptor, Drug.**

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KATHRYN A. CUNNINGHAM

SEXUALITY AND SUBSTANCE ABUSE.

The interplay of sexuality and the use of alcohol and drugs is manifest in images as old as Bacchus, allusions to "wine, women, and song," and its modern transformation "sex, drugs, and rock-and-roll." The impact of alcohol on sexuality most commonly evokes images of Bacchanalian toga parties. Fears of "reefer madness" included alarms of unleashed licentiousness. The popular belief is that psychoactive substances loosen sexual inhibitions leading to increased sexual activity.

The purpose of this discussion is to explain the complex interaction between human sexual expression and the nonmedical social uses of intoxicating substances. Topics to be broached will include the specific effects of psychoactive substances on sexual function, the use of drugs to facilitate sexual behavior, and the association of drug use with high-risk sexual behavior. Peugh and Belenko (2001) provided a critical review of the research on the impact on human sexual function of acute and chronic substance use. The literature included controlled laboratory studies as well as survey and interview techniques.

DIFFICULTIES IN RESEARCH

Research typically characterizes sexual function as a physiological event by distinguishing between libido and sexual interest, arousal (erection in males; lubrication in females), ability to orgasm, and intensity of and emotional sense of satisfaction from the orgasm. In humans this complex biologic event is shaped by the individual's genetics, psychology, and previous history, as imbedded in an environmental and cultural milieu. Consequently, from a research point of view, the difficulty in controlling for these factors with sample sizes of sufficient number makes drawing conclusions a daunting task. In the face of the limitations in research methodology, Peugh and Belenko found sufficient evidence for harmful effects on sexual functioning. A 2007 study published in the United Kingdom (Sumnall, Beynon, Conchie, Riley, & Cole, 2007) suggested that sexual activity after drug use was most frequently circumstantial and associated with cannabis and MDMA (Ecstasy). When used intentionally to facilitate a sexual encounter, the effects of these drugs were to lower inhibitions, raise self-confidence, and give a greater perception of interpersonal contact with the partner.

ALCOHOL AND SEXUAL RESPONSE

Beckman and Ackerman (1995) noted that while many women acknowledge a subjective increase in sexual desire and pleasure with alcohol, it lowers physiological arousal and leads to a change in sexual behavior in few women. In 2007 Schacht and colleagues reported a fascinating study comparing the effects of alcohol intoxication on psychophysiological measures of sexual responding. Two groups of women, distinguished by the presence or absence of a history of having been sexually abused, were monitored in their response to erotic films. Women who had suffered sexual abuse reported more sexual arousal in the intoxicated state

than when sober. They had higher mood ratings when intoxicated and were not able to suppress their sexual response to erotic films when given this instruction. Women without an abuse history demonstrated a decrease in sexual arousal and maintained their ability to suppress their sexual response when given this instruction while intoxicated. These findings are particularly germane to the association of heightened risk of sexual dysfunction in women with alcohol problems who have experienced childhood incest or sexual assault. It raises the possibility that early abuse resets the nervous system to experience alcohol hedonically as a mood enhancer and sexual disinhibitor. This could increase a woman's risk for both alcohol problems and high-risk sexual behavior.

Abbey and colleagues explored the acute effects of alcohol on sexual decision-making in men and women. The researchers used a laboratory paradigm of instructing subjects to read or listen to a vignette while sober and while intoxicated. When reviewing the dating vignette while intoxicated, both genders misread active attention as sexual interest and exaggerated dating availability cues as being sexually provocative. Extending the paradigm to date rape vignettes gave results in which, while intoxicated but not while sober, both genders failed to identify the inappropriateness of the man's sexual behavior and consistently overrated the level of the woman's sexual arousal. In a further experiment, the paradigm was used to demonstrate that intoxicated subjects were more likely than their sober cohort (matched study group) to expect unprotected sexual intercourse in a vignette of a couple contemplating sex without condoms.

DRUGS AND SEXUAL RESPONSE

The literature on opioids, notably, has minimal reference to opioids as enhancing sexual arousal or functioning. In a 2008 study from Australia (Hallinan et al., 2008), men on methadone had a high prevalence of erectile dysfunction related to hypogonadism compared to men on buprenorphine. A large study from Taiwan in 2007 (Bang-Ping, 2007) reported 46.7 percent of heroin users had diminished libido and erectile dysfunction. A study in Michigan in 2005 (Brown et al., 2005) also noted erectile and orgasmic dysfunction in a group of methadone patients.

In 2003 El-Bassel and colleagues reported on 38 women in methadone treatment who were interviewed because they acknowledged abuse by their drug-involved partners. Of note was the frequent report that male and female partners experienced the opposite sexual response to the same shared drug, which led to sexual coercion and violence. For example, many of these women experienced a decrease in sexual arousal with cocaine, whereas their male partner experienced increased sexual and aggressive arousal.

The malignant dynamics of sexual expression and drug use came to the fore during the crack cocaine epidemic in the 1980s and 1990s. In 1991 Marx reviewed sixteen epidemiological studies that examined drug use, sexual behavior, and sexually transmitted disease (STD). The exchange of sex for money or drugs was associated with STDs in seven studies. Eight studies found an association between crack and STDs. The exchange of sex for crack cocaine was both a rural and urban problem. Dramatic increases in juvenile delinquency and STDs among inner city teenagers were reported (Fullilove et al., 1993). Teenagers using crack were more likely to have sexual intercourse under the influence of drugs and alcohol, to engage in sex in exchange for money or drugs, and to have more sexual partners. These findings were true for both males and females.

A comparison of crack-abusing to opioid-abusing women revealed higher rates of high-risk sexual behavior including prostitution, infrequency of condom use, and a greater number of sexual partners in the crack-abusing women. The opioid-abusing group had a much greater proportion of high-risk behavior associated with needle use (Cohen et al., 1994).

Despite the consistent findings of high rates of risky sexual behavior in crack-abusing women, Henderson and colleagues (1995) found no evidence that these women found crack to be an aphrodisiac. To the contrary, they found high rates of sexual dysfunction. Recent studies have corroborated this finding, identifying the need to acquire money for drugs to avoid withdrawal, rather than increased libido, as the impetus to sexual behavior. DeBeck and colleagues reported in 2007 that 62 percent of women engaged in the sex trade would give up the illegal services if they did not need money for drugs. The need for drug money

frequently overpowers the determination to insist on condom use as well. The phenomenon of sex-for-crack is most rampant in the crack house itself (Inciardi, 1995). Some studies report 30 percent of the men and 90 percent of the women had one hundred or more sexual partners within thirty days of being interviewed for the study. As might be expected, individuals described as crack-smoking drug injectors carried the highest risks of STD and HIV seropositive states. They also had the highest frequency of having a drug-injecting sex partner, multiple sex partners, low rates of condom use, and high rates of alcohol consumption and were more likely to exchange sex for drugs.

The health consequences of injection drug use and cocaine smoking show little signs of abating. HIV seropositive rates in 3,555 urban and rural Florida drug users and controls as reported by McCoy in 2004 were 7.3 percent of those in the control group, 20 percent of crack smokers, 30 percent of crack-smoking injectors, and 45 percent of injection-only drug users. In 2006 the emergence of injecting crack cocaine was described in Connecticut and Massachusetts, revealing even higher rates of risky sexual behavior and health consequences reported than with "speedball" (powder cocaine and heroin) injections or powder cocaine injections alone (Buchanan et al., 2006).

EFFECTS OF CLUB DRUGS

The burgeoning use of the group of drugs labeled by the National Institute on Drug Abuse [NIDA] as *club drugs* has raised widespread concern. The following drugs are included: methamphetamine, MDMA, amyl nitrate, LSD, GHB, rohypnol or flunitrazepam, and ketamine (Wu et al., 2006). These compounds are named for the context of their use, rather than for any chemical composition or biological activity. They are used recreationally at social events, like music festivals, nightclubs, circuit parties, and raves to enhance energy, endurance, sociability, sexual arousal, or to create an altered state of consciousness with heightened sensory stimulation. These compounds are generally low cost, conveniently distributed as small pills, powders, or liquids, and are perceived as safe by users.

The association between sexual activity and club drug use was initially described in the homosexual community in the 1990s. Most studies of club drug use have focused on adult sub-populations, for example, gay, bisexual, substance abusers, club/party participants who acknowledge drug use. In all studies, regardless of sample characteristics, the recurrent findings are of polydrug use, excessive high-risk sexual behavior, high frequency of substance abuse disorders, and STD and HIV transmission (Colfax et al., 2005; Halkitis et al., 2005; Rawstorne et al., 2007).

METHAMPHETAMINE USE

Studies of methamphetamine use in male gay populations frequently noted the pattern of methamphetamine, Viagra, and either amyl nitrate, GBH, or ketamine (Crosby and DiClemente, 2004; Spindler et al., 2007; Carey et al., 2008). Some users acknowledged wishing for "better, longer, harder sex." Unfortunately, the association of the use of such cocktails with the prevalence of HIV-positive sero-status and unprotected oral, anal, and anonymous sex is consistently high. Users acknowledge the yearning to combat loneliness, fears about the loss of physical attractiveness due to aging and illness, the psychological stress about HIV status, and the physical discomfort of the sexual act as predominant reasons for using these drugs (Kurtz, 2005).

Methamphetamine and MDMA are related in their chemistry to amphetamine. The subtle molecular differences of MDMA confer pharmacologic properties similar to the hallucinogen mescaline. This may be responsible for the differences reported in the subjective experiences of *crystal* and *Ecstasy* (Kalant, 2001). Both promote alertness and energy, but Ecstasy confers a euphoria, increased sensory awareness, enhanced emotional closeness, and intimacy. Zemishlany and colleagues (2001) reported on the subjective evaluation of sexual functioning in 35 recreational Ecstasy users. Desire and satisfaction were moderately to profoundly increased in 90 percent of subjects. Orgasm was delayed, but perceived as more intense. However, physiological arousal was impaired in 40 percent of the men.

There has been speculation that methamphetamine differs from other club drugs in relation to risky sexual behavior and the pattern of sexual arousal (Schilder et al., 2005). Studies have shown crystal users, whether homosexual or heterosexual, male or female, are consistently and significantly

more likely to engage in high-risk sexual behaviors. Studies from Australia (Rawstorne et al., 2007), New York (Halkitis et al., 2005), and San Francisco (Colfax et al., 2005) suggest a more nuanced notion that different molecules may carry different risks to different groups. It is certainly conceivable that methamphetamine may separate itself in its capacity to precipitate devastating addiction cycles with consequent unsafe behaviors as a by-product, as seen in the crack-for-sex epidemic.

MDMA is by no means benign, as serious acute and chronic toxicities have been demonstrated. Adverse medical events and fatalities consistent with syndromes of excess neurotransmitter levels are being observed with increasing frequency (Kalant, 2001). There is increasing concern that long-term MDMA neurotoxicity leads to persistent neuropsychiatric difficulty, even after accounting for polydrug use and preexisting neuropsychological state (Gouzoulis-Mayfrank et al., 2006; Thomasius et al., 2006).

LSD is the most widely used hallucinogen among adolescents and is associated with risky sexual behavior and heavy alcohol use (Golub et al., 2001). Ketamine is an anesthetic agent with effects similar to phencyclidine, though of a much shorter duration. Flunitrazepam (rohypnol, "ruffies") and GHB ("liquid X") are both potent sedative-hypnotics. Ketamine, rohypnol, and GHB have been implicated with alcohol in the increasingly prevalent problem of drug-facilitated sexual assault.

Wu's (2006) published results from the National Survey of Drug Use and Health revealed 20 percent of the participants acknowledged using one or more club drugs. Eighty percent of the children studied used three or more drug classes. Club drug use was highly associated with criminal behavior and recent alcohol abuse or dependence.

Of fundamental importance in stressing and assessing the danger of club drugs is the consistent pattern of polydrug use in venues of extreme crowds, excess physical activity, and elevated temperatures with molecules of unknown purity whose toxic dose range and recreational dose range merge precariously (Parrott, 2006).

DRUGS AND SEXUAL DEVELOPMENT

The 1993 Massachusetts Youth Risk Behavior Survey of 3,000 students found a significant association between early onset of sexual intercourse and higher number of sexual partners with the early onset use of marijuana, cocaine, crack, and alcohol (Shrier et al., 1997). Staton and colleagues (1999), in a study of 952 young adults in Lexington, Kentucky, replicated the finding of earlier initiation of sexual activity being related to the early use of drugs. A 2001 survey reported that California youth in substance abuse treatment had an earlier age of onset of sexual activity, more partners, less use of condoms, more STD, more HIV-positive results, and more pregnancies (Tapert et al., 2001). Studies published in 2002 of 808 Seattle children, surveyed at age 10 in 1985 and followed to age 21 in 1996, found that binge drinkers and marijuana users had more sex partners and were less likely to use condoms consistently, as compared to their abstinent peers (Guo et al., 2002). In 1993 Fullilove and colleagues, reporting on crack-abusing inner city adolescents, found that almost 50 percent had sexual intercourse while intoxicated, and that 29 percent of boys and 25 percent of girls engaged in sex for drugs or money.

G. La Pera has authored a series of papers describing the increased incidence of sexual dysfunction and the impact this sexual dysfunction had on the original decision to use drugs in young Italian men who later developed substance abuse disorders. This raises the consideration that sexual dysfunction can be both a precipitant and a consequence of substance abuse disorders

In 2000 M. A. Bellis published the results of a survey of 1,340 16 to 35-year-olds from nine European cities. He explored the strategic roles for which young people utilize substances to facilitate sex. He found that 29 percent of alcohol users hoped to facilitate encounters, and 26 percent of cocaine users hoped to prolong sex. Substance abuse before 16 years of age consistently was associated with sex before 16 years of age. Previous studies by Bellis revealed that young adults traveling on holiday to European hot spots increased their drug use and at-risk sexual behaviors significantly. He also reported on the significant recruitment of new users of drugs during these vacations.

The catastrophic synergy between substance abuse and high-risk sexual behavior and the epidemic of sexually transmitted diseases has absorbed the energies of health care providers, researchers,

and policymakers for decades. It has become evident that the use of psychoactive substances plays a significant role in the emergence of sexual victimization and violence. Nonetheless, it is the increasingly frequent early initiation of drug and alcohol use by youth and the concomitant emergence of high-risk sexual activity that is most troubling. M. A. Bellis described the problem as follows:

> An epidemic of recreational drug use and binge drinking exposes millions of young . . . to routine consumption of substances which alter their sexual decisions and increases their chances of unsafe and regretted sex. For many, substance use has become an integral part of their strategic approach to sex, locking them into continued use. Tackling substances with both physiological and psychological links to sex requires approaching substance abuse and sexual behavior in the same way that individuals experience them; as part of the same social process (Bellis et al., 2008).

See also **Alcohol: Chemistry and Pharmacology; Childhood Behavior and Later Substance Use; Club Drugs; Complications; Epidemics of Drug Abuse in the United States; Gender and Complications of Substance Abuse; Injecting Drug Users and HIV; Intimate Partner Violence and Alcohol/Substance Use; National Survey on Drug Use and Health (NSDUH); Neurotransmitters; Opiates/Opioids; Polydrug Abuse; Psychoactive; Rave; Research: Measuring Effects of Drugs on Behavior; Risk Factors for Substance Use, Abuse, and Dependence: Sexual and Physical Abuse; Sensation and Perception and Effects of Drugs; Substance Abuse and AIDS.**

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GERSON M. STERNSTEIN

SHISHA. *See* **Hookah.**

SHOCK INCARCERATION AND BOOT-CAMP PRISONS. Shock incarceration programs, or boot-camp prisons, are short-term prison programs for young offenders that are modeled on military basic training programs. Since they were first established in 1983, all the U.S. states and many U.S. counties have adopted this type of program. Boot-camp prisons have proved to be controversial, however, and critics argue that this type of regimen does not reduce recidivism (the tendency to return to crime after release). In the late 1990s, allegations of misconduct and abuse by boot-camp prison staff members against their juvenile inmates led to criminal investigations and the closing of facilities. Nevertheless, this type of "tough love" approach remains a popular option for some correctional officials.

Those sentenced to boot-camp prisons are required to arise early each day to participate in a rigorous schedule of physical training, military drill and ceremony, and hard labor. While they are in the boot camp, participants are separated from other prisoners. They are allowed few personal possessions, no televisions, and infrequent visits from relatives on the outside.

The correctional officers in the programs are referred to as drill instructors and are responsible for seeing that the inmates obey the rules and participate in all activities. When speaking to staff, inmates must refer to themselves as "this inmate" and they must proceed and follow each sentence with "sir" or "madam," as in the familiar military response, "Sir, yes, sir." Disobedience is punished immediately using summary punishments, frequently in the form of some additional physical activity, such as push-ups or sit-ups. More serious rule violations may result in dismissal from the program.

BOOT-CAMP PRISONS AS INTERMEDIATE SANCTIONS

The boot-camp prisons were developed during the 1980s, partly in response to the phenomenal growth in the number of convicted young offenders. There were only two options in managing this population—either they were sent to prison or they were supervised in the community on probation. Neither option was entirely satisfactory for the large number of young offenders, however. Correctional jurisdictions faced severe prison overcrowding, and probation caseloads grew so large that many offenders received only nominal supervision during their time in the community. Alternative sanctions or intermediate punishments were proposed, such as intensive community supervision, house arrest, or residential-community corrections centers. These options provided more control than a sentence to probation but less than a sentence to prison. Boot-camp prisons were one relatively inexpensive alternative sanction that became particularly popular.

The first boot-camp prisons were begun in 1983 in Oklahoma and Georgia. These two programs attracted a great deal of attention, and other jurisdictions soon began developing similar programs. By 1999, more than 50 boot camps housed about 4,500 juveniles. Although the majority of the camps have male participants, some programs admit women as well, and some states developed completely separate boot-camp prisons for women. The Federal Bureau of Prisons developed one boot camp for males and a separate program for females. Despite this initial popularity, by 2000 various problems and doubts had led several states to either end their programs or drastically scale back the size of the programs.

ENTERING AND EXITING

Because most boot camps have strict requirements about who is eligible, inmates are carefully evaluated prior to being sent there. Most programs require participants to sign an agreement saying

Prisoners entering "Boot Camp" in Sumter County Correctional Institution. © BETTMANN/CORBIS.

they have volunteered. They are given information about the program and the difference between a boot-camp prison and a traditional prison. The major incentive for entering the boot camp is that the inmate serves a shorter term than under a traditional prison sentence.

The first day of the boot camp involves a difficult in-take process, during which the drill instructors confront the inmates. Inmates are given rapid orders about the rules of the camp, including when they can speak, how they are to address the drill instructors, and how to stand at attention. The men have their heads shaved, and the women receive short haircuts. This early period in the camp is physically and mentally stressful for most inmates.

The programs last from 90 to 180 days. Those dismissed prior to graduation are considered program failures, and they are either sent immediately to a traditional prison to serve a longer term of incarceration or they are returned to court for resentencing. Offenders who successfully complete the boot camp are released. After graduating, they are supervised in the community for the rest of their sentence. There is usually an elaborate graduation ceremony during which inmates demonstrate the military drills they have practiced. Many programs encourage family members to attend the graduation ceremony.

A DAY IN BOOT CAMP

On a typical day, the participants arise before dawn, dress rapidly, clean their living quarters, and march in cadence to an exercise area, where they will spend an hour or more doing calisthenics and running. They then march back to their quarters for a quick cleanup before breakfast. As they do at every meal, they march to breakfast and stand at parade rest while waiting to be served. They stand at attention until ordered to sit and eat without conversation. Following breakfast they may work for up to six or eight hours. This is usually hard physical labor, such as cleaning state parks or public roads. They return in the late afternoon for additional physical exercise or practice in drill and ceremony. After a quick dinner, they attend rehabilitation programs until 9 p.m., when they return to their dormitories. In the short period before bedtime, they have time to be sure their shoes are shined and their clothes are clean and ready for the morning.

DRUG TREATMENT IN THE BOOT CAMP

The earliest boot camps focused on discipline and hard work. More recently, they have begun to emphasize treatment and education. It became clear that many of the entrants were involved with drugs. Realizing that punishment alone would not effectively reduce the drug use of these offenders, corrections officials introduced drug treatment or education into the daily schedule of boot-camp activities. By the late 1980s, all the camps had some type of substance abuse treatment or education (MacKenzie, 1994).

As with other aspects of the programs, the type of treatment and the amount of time devoted to substance abuse treatment varies greatly among programs. The 90-day Florida program includes only 15 days of treatment and education, while the New York program provides 180 days of treatment.

Most programs have reported that drug use is monitored during community supervision, the schedule and frequency of this monitoring varies greatly.

SIMILARITIES AND DIFFERENCES

All the boot-camp prisons incorporate the core components of military basic training, such as physical training and hard labor. Most target young offenders convicted of nonviolent crimes such as drug, burglary, or theft. Participation is limited to those who do not have an extensive past history of criminal activity. Other than these similarities, the programs differ dramatically. Some focus only on work, military drill, and exercise. In other boot camps, offenders spend a great deal of time each day in rehabilitation programs. The camps also differ in the type of the therapeutic programming provided. Some emphasize academic education, while others focus on group counseling or treatment for substance abuse.

The boot camps also differ in the ways offenders are managed after release. Some programs intensively supervise all the offenders who successfully complete the boot camp; others are supervised as they would be in traditional probation caseloads. Program officials worry about the difficulty the graduates have in making the transition from the rigid structure of the boot camps to the community environment. For this reason, some boot camps developed aftercare programs to help them make the change. These aftercare programs do more than increase the surveillance of the activities of the graduates. They are designed to provide drug treatment, vocational counseling, academic education, and short-term housing.

New York's Therapeutic Community Boot Camps. Among the boot camps that include substance abuse treatment as a component of the in-prison phase of the program, there are large differences in the way this treatment is delivered. The boot-camp programs developed by the New York Department of Correctional Services use a therapeutic community (TC) model. All offenders are given a similar regimen of drug treatment while they are incarcerated. Each platoon in the camp forms a small community, and they meet daily to solve problems and discuss their progress in the shock program. They spend over 200 hours during the six-month program in a substance-abuse treatment program based on the Alcoholics Anonymous (AA) and Narcotic Anonymous (NA) models of abstinence and recovery. All the inmates participate in the treatment, regardless of their history of use and abuse.

Illinois's Boot Camp with Levels of Treatment. Like New York, the Illinois boot camp also targets substance abusers. However, the delivery of treatment services is very different. In Illinois, counselors evaluate offenders and match the education and treatment level to the identified severity level of the offender. Three different levels of treatment are provided. Inmates identified as level one have no substance abuse history, and therefore they receive only two weeks of education. Level-two inmates are identified as probable substance abusers. They receive four weeks of treatment in addition to the drug education. The treatment consists of group therapy focusing predominately on denial and family-support issues. Inmates identified as level three are considered to have serious drug addictions, and they receive ten weeks of education and treatment. In addition to the drug education and group therapy, they receive group sessions on relapse, codependency, behavioral differences, family addiction, and roles within the family.

Texas's Voluntary Participation Model. A third model is represented by the Texas program (MacKenzie, 1994). In the boot camp, all participants receive five weeks of drug education. During this phase, inmates may also receive individual counseling and attend twelve-step fellowship meetings. More drug treatment is available for those who volunteer (the substance abuse counselors in this program believe that treatment should be voluntary). These volunteers receive approximately four hours per week of treatment in the form of group therapy. The meetings are held during free time, so inmates are not released from work to attend. The group sessions focus on social values, self-worth, communication skills, self-awareness, family systems, self-esteem, and goal setting. Some inmates also receive individual counseling.

DISMISSAL RATES

As occurs in many drug-treatment programs, boot camps may have high dismissal rates. Depending upon the program, rates vary from 8 percent (Georgia in 1989) to as much as 80 percent (Wisconsin in

1993). Offenders can be dismissed from the boot camp because of misbehavior, and in some boot camps they can voluntarily ask to leave. Those who are dismissed will either be sent to a traditional prison, where they will serve a longer sentence than they would have in the boot camp, or they will be returned to the court for re-sentencing. Thus, in both cases, there is the threat of a longer term in prison for those who do not complete the boot-camp program.

There is very little information about how drug-involved offenders do in boot-camp prisons. One study of the Louisiana boot camp compared the dismissal rates of drug-involved offenders with the rates of offenders who were not identified as drug-involved (Shaw & MacKenzie, 1992). Two groups of drug-involved offenders were examined: those who had a legal history of drug-involvement (an arrest or conviction for a drug offense), and those who were identified as drug abusers on the basis of self-report. In this program, offenders were permitted to drop out voluntarily or they could be dismissed for misbehavior. Surprisingly, in comparison to other offenders, the drug-involved offenders were less likely to drop out of the program.

In another study of the Louisiana boot camp, 20 percent of the participants were identified as problem drinkers on the basis of their self-reported alcohol use and problems associated with use (Shaw & MacKenzie, 1989). The problem drinkers were no more likely to drop out of the boot-camp prison than were other inmates.

In interviews, offenders who are near graduation from boot camp report that they are drug free and physically healthy (MacKenzie & Souryal, 1994). Unlike offenders incarcerated in conventional prisons, boot-camp participants tend to believe that their experience was positive and that they have changed for the better. They also report that the reason they entered the boot camp was because they believed they would spend less time in prison—not because of the treatment or therapy offered.

PERFORMANCE DURING COMMUNITY SUPERVISION

Studies have compared the performance of boot-camp graduates during community supervision with those who served a longer time in prison or were sentenced to probation. In most cases, there were no significant differences between these offenders in recidivism rates or in positive social activities (MacKenzie & Souryal, 1994). One study used a statistical technique called meta-analysis to examine the results from 43 different studies of correctional boot camps. All these studies compared the recidivism of boot-camp participants with those who served other sentences (MacKenzie, 2007; Wilson et al., 2008). Overall, the findings were that the recidivism rate of boot-camp participants was almost identical to the recidivism rate of similar offenders who served different sentences. The researchers concluded, therefore, that boot camps are not effective in reducing recidivism. However, there was some suggestion in the studies that boot camps with more treatment and therapy in the daily schedule of activities may reduce recidivism. For example, boot-camp graduates in Illinois and Louisiana had fewer revocations for new crimes. Research examining New York offenders found mixed results. Graduates had fewer new crime revocations in one study (New York State Department of Correctional Services, 1994) and fewer technical violations in another study (MacKenzie & Souryal, 1994).

If the military atmosphere alone changed offenders, all the graduates would be expected to have lower recidivism rates and a better positive adjustment. The inconsistency of the results suggests that the boot-camp atmosphere alone will not successfully reduce recidivism or positively change offenders. Some other aspects of the Illinois, New York, and Louisiana programs, either with or without the boot-camp atmosphere, led to the positive impact on these offenders. After an examination of these programs, the researchers concluded that: (1) all three programs devoted a great deal of time to therapeutic activities, (2) a large number of entrants were dismissed, (3) the length of time in the boot camp was longer than other boot camps, (4) participation was voluntary, and (5) the in-prison phase was followed by six months of intensive supervision in the community. However, it was not possible to separate the effect of these components from the impact of the military atmosphere. Most likely, the therapy provided during the program and the transition and aftercare treatment provided during community supervision are critical components of the program for drug-involved offenders. It is not known if a drug treatment program without a

boot-camp atmosphere would be more or less effective than drug treatment within a boot camp.

PERFORMANCE OF DRUG-INVOLVED OFFENDERS

Shaw and MacKenzie (1992) studied the performance of drug-involved offenders during community supervision in Louisiana. In comparison to offenders who were not drug-involved, these individuals did not do as well during community supervision. This was true of those on probation, parolees from traditional prisons, and parolees from the boot camp. Thus, the boot-camp parolees did not do better than those from other settings. During the first year of supervision, the drug-involved offenders were more likely to have a positive drug screen.

Problem drinkers who graduated from the Louisiana program were found to perform better, as measured by positive activities during community supervision (Shaw & MacKenzie, 1989). Their performance was, however, more varied, indicating that they may need more support and aftercare than other offenders. In contrast to the Louisiana findings, research in New York indicated that those who were returned to prison were more apt to be alcoholics (New York Department of Correctional Services, 1994). In both Louisiana and New York, offenders who were convicted of drug offenses did better than self-confessed alcoholics during community supervision.

THE FUTURE OF BOOT-CAMP PRISONS

Boot-camp prisons are still controversial. By the late 1990s, skepticism had risen about the effectiveness of this approach. Studies conducted for the U.S. Justice Department found that the national recidivism rate for boot camps ranged from 64 to 75 percent. This compared to recidivism rates from 63 to 71 percent for those who served their time in traditional detention centers. Although juveniles often responded well while in the camps, they returned to the same neighborhoods where they first got into trouble. Furthermore, news reports of abuse, injuries, and deaths in the camps led many correctional administrators to be wary of initiating new shock incarceration programs. Colorado, North Dakota, and Arizona ended their programs, and Georgia, where boot-camp prisons started, is phasing out its camps.

People are concerned that inmates' rights will not be observed in boot-camp prisons, and that inmates are being coerced to do something that is not good for them (Morash & Rucker, 1990). These critics argue that the summary punishments and the staff yelling at offenders may be abusive for inmates; that participants may leave the boot-camp prison angry and damaged by the experience; and that the military atmosphere, which is designed to create a cohesive fighting unit, may not be appropriate for young offenders. These concerns became public in the late 1990s, as state and federal prosecutors investigated allegations of abuse and misconduct by prison camp staff. Maryland fired its top five juvenile-justice officials in 1999 after officials investigated reports of systematic assaults at three boot-camp prisons.

Advocates of boot camps say that these programs have many benefits. In their opinion, these offenders lack the discipline and accountability that are provided by the program. Furthermore, they argue, the strong relationship between the offenders and the drill instructors may be helpful to the inmates, and that there may be some aspects of the boot camps that are particularly beneficial for drug-involved offenders. Thus, although controversy exists about the boot-camp prisons, they remain a popular alternative sanction.

See also **Civil Commitment; Coerced Treatment for Substance Offenders; Criminal Justice System, Treatment in the; Narcotic Addict Rehabilitation Act (NARA); Prisons and Jails; Treatment: An Overview.**

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SLANG TERMS IN U.S. DRUG CULTURES. Because illicit drugs (and prescription drugs used in ways other than intended) are illegal, those who use them, and those who live within the drug culture, develop their own communication system—both for self-protection and as a means of identifying others within the group. This is the case for several marginalized underworld subcultures, such as street gangs, prison gangs, and incarcerated individuals. The argot, or slang, of drug users is this specialized vocabulary or the collection of words and phrases used by one drug user to communicate with another—often to the exclusion of non-users. In some instances, this argot extends to the intonation or pitch used to speak words and phrases.

Argot fascinates sociologists, anthropologists, and others who study human behavior because its use is an example of learned behavior that helps identify members of a particular social or cultural group. Alfred Lindesmith did substantial field research to create and verify his lexicon, recorded in his well-known 1938 essay "Argot of the Underworld Drug Addict."

A. M. Smith and colleagues studied more than 2,000 drug users in Baltimore, Maryland, in 1992. Subjects were shown a photograph of someone injecting a drug into his vein and asked, "What do you call this?" More than 50 percent identified the photo as an image of someone *firing up*; the others called it *shooting*. Most other people in Baltimore speak of *firing up* their furnaces or *shooting* baskets on a basketball court, but they do not think about drug use when these terms are used.

The argot of drug users also varies from place to place and from time to time. A very small minority of drug users in Smith's study spoke of *mainlining* the drug, *spiking*, or *oiling* when they looked at a photo of drug injection into a vein. These are older terms for the same injecting behavior called *firing up* and *shooting* by younger drug users.

In some ways, argot reflects the social structure of groups: In-group members use the argot, whereas others do not. However, if argot serves as a badge of membership in an in-group, then one might expect to hear it in general conversations, no matter who is present. Nonetheless, sociologists studying the use of argot often have been surprised to find that it is spoken mainly among group members but not as frequently when nonmembers are present.

Arguing from evidence of this type, some observers claim that argot serves more to convey and reinforce identities within groups than to distinguish one group from another. That is, the process of learning and using drug-related argot reinforces the experience of joining in with others who use drugs. In some ways, this process might

Term	Definition
a	amphetamines, a stimulant
a-bomb, *bomb*	LSD, a hallucinogen
acid	[a shortening of *d*-lysergic acid diethylamide; since about 1960] LSD
Adam	[originally named to connote a primordial man in a state of innocence] MDMA, a mild hallucinogen. *See* Ecstasy below.
amp	[from *ampoule*; the drug is sold in small glass ampoules, which are broken open and the contents inhaled] amyl nitrite, a dilator of small blood vessels and used in medicine for angina pains; used illicitly to intensify orgasm or for a stimulation effect
amps	amphetamines
angel dust	[since the 1970s] phencyclidine (brand-name Sernyl), an anesthetic used on animals but originally on humans; discontinued because of bizarre mental effects. *See* PCP below.
Are you anywhere?	"Do you use marijuana?"
author	medical professional who writes illegal prescriptions
bagging	taking an inhalant by breathing it from a bag
base	The pure alkaloid of cocaine that has been extracted from the salt (cocaine hydrochloride), in the form of a hard white crust or rock. *See* crack and rock below.
batu	crystalline methamphetamine
beamed up	[from "Beam me up, Scotty," an expression used in the television series *Star Trek*] intoxicated by crack
beamer	a crack addict
beans	dextroamphetamines
beast	LSD
beat	[from the idea of beating or cheating someone] a bogus or mislabeled drug or substance resembling a certain drug and sold as that drug (soap chips as crack; methamphetamine or baking soda as cocaine; catnip as marijuana; PCP as LSD, mescaline, or tetrahydrocannabinol (THC, the active principle of marijuana); procaine as cocaine)
big C	cocaine
big H	heroin
black beauties	amphetamines
black tar	heroin
blank	nonpsychoactive powder sold as a drug
blast	a drag of crack smoke from a pipe
blotter	[doses of the drug are dripped on a sheet of blotter paper for sale] LSD
blow	(1) to sniff a drug. (2) cocaine. (3) to smoke marijuana (*to blow a stick*).
blue heavens	methaqualone (a sedative) pills
blue lips	use of MDMA
bone	a marijuana cigarette; a joint
boom	marijuana
boomers	hallucinogenic mushrooms containing psilocybin
booze	alcohol
bottles	vials or small containers for selling crack
boy	heroin
breakfast cereal	ketamine. *See* K below.
brown	heroin from Mexico diluted with brown milk sugar (lactose), which is less pure than China white. Also called Mexican mud
brown sugar	heroin
buds	[from its appearance] marijuana or sinsemilla (a hybrid variety of marijuana); a quantity for sale consisting mainly of the more potent flowering tops of the marijuana plant (Cannabis sativa). *See* sinse below.
bump	(1) cocaine. (2) crack. (3) fake crack. (4) hit of ketamine. *See* K below.
bush	[from *righteous bush*] marijuana
bust	[from 1930s Harlem slang for a police raid, perhaps a shortened form of *busting in*] arrest
button	[from the shape of the appendages to the peyote cactus containing mescaline] peyote or San Pedro cactus
buzz, *buzzed*	[from *buzz*, onomatopoeic equivalent of subjective feeling; the onset of the drug sometimes causes buzzing in the ears] (1) high on marijuana. (2) an inferior high from heroin.
C	cocaine
candy	cocaine
caps	hallucinogenic mushrooms
chalk	[from its appearance] crystal methamphetamine or cocaine
Charlie	cocaine
chasing the dragon	[from a Chinese expression for inhaling the fumes of heroin after heating it; the melting drug resembles a wriggling snake or dragon] (1) inhaling heroin fumes after the substance is heated on a piece of tinfoil. (2) smoking a mixture of crack and heroin.
cheba	marijuana
China white	[from China (Indochina) white or white stuff = heroin; since the 1970s] (1) relatively pure heroin from Southeast Asia. (2) analogues of fentanyl (Sublimaze), an opioid more potent than heroin and sold on the street as China white.
chipping, to chippy	using heroin occasionally, avoiding addiction
chronic	marijuana
cocoa puff	[pun on the name of a chocolate-flavored breakfast cereal] a joint, to which cocaine has been added
coke	cocaine
cola	[a word play on *coke, cocaine*, and *Coca-Cola*, cocaine is derived from the coca (not the kola) plant] cocaine
cold turkey	[from the gooseflesh that is part of abrupt withdrawal] by extension, ending a drug habit without medicinal or professional help, *going cold turkey*
coming down	[from a *high*] losing the effects of a drug, all the way down to crashing
connect	[from the *connection*, a drug pusher] cocaine importer or wholesaler, who fronts (consigns) cocaine to a supplier, who in turn distributes to a street retailer. *See* dealing, mule, runner, steerer, touting.
cop	[from British slang of the 1700s; to obtain, to steal, to buy; since the 1890s] to get or purchase illicit drugs
cop a buzz	get high

[CONTINUED]

Table 1. Slang terms. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Term	Definition
copping zone	an area where drugs are sold
crack	[from the crackling sound when smoked in a pipe] pebbles of cocaine base that are smoked
crack house	house or apartment (sometimes, an abandoned building) where crack cocaine is sold and smoked on the premises 24/7—twenty-four hours a day, seven days a week
crank	crystal methamphetamine
crank lite	[from *crank*, because of the amphetaminelike stimulant effect, + *lite*, meaning "lighter," as in low-alcohol beer] ephedrine, a stimulant used in nonprescription medicines such as a decongestant, which is lighter than amphetamines
crash, *crashing*	to come all the way down from a drug high
cross roads	[from the scored cross on the tablets] amphetamines
crystal	[in powder form] methamphetamine or cocaine
crystal supergrass	marijuana with PCP
cut	to add adulterants to a drug, extending it to make more money on its sale (some adulterants are relatively harmless, some toxic)
date rape drug	Rohypnol, called roofies. At a party this tasteless, odorless drug may be slipped into a woman's drink. After she loses consciousness, she may be raped and later have no memory of the incident.
deadeye	blank stare produced by an overdose of phencyclidine (PCP) or another drug
dealing	[from *dealer*, a person who sells drugs; since the 1920s] selling drugs of all kinds
designer drugs	synthetic compounds or drug analogues that produce the effects of certain regulated drugs but have slight differences in chemical composition to evade regulatory law, e.g., analogues of fentanyl (China white); analogues of amphetamine and methamphetamine, such as MDA, MDMA (Ecstasy), TMA, MMDA, MDE (Eve), MBDB; toxic by-products of the synthetic opiate meperidine (Demerol), such as MPTP and MPPP dexies: dextroamphetamines
devil's dandruff	crack or powder cocaine
ditch	veins on the inside of the arm at the elbow, a site for injecting heroin.*See* tracks below.
do drugs	take or use illicit drugs
doobie	a marijuana cigarette; a joint
dope	[from Dutch *doop*, meaning "sauce" (from *dopen*, "to dip"). In the late19th century the term came to be applied to opium, a black gum shaped into pellets and smoked in a pipe] (1) drugs. (2) marijuana. (3) heroin and other illicit drugs. (4) intoxicating fumes of airplane fuel or glue. (5) Coca-Cola.
dope fiend	[opprobrious term for users of narcotics and illicit drugs since the early 1900s; the term is used ironically by drug users to defy the social stigma] drug user, drug abuser, drug addict
dosing	slipping a hallucinogenic drug into punch, brownies, etc., so that it will be consumed unwittingly by others
downer	barbiturates
drag	to draw or pull on smoke from a cigarette, pipe, or other item (*to take a drag*); to convey that smoke into one's throat and lungs *See* toke below.
drop	to swallow LSD or a pill
dugie, *doojee*	[phonetic] heroin
dust	PCP
dusting	(1) mixing either cocaine with tobacco in a cigarette, or heroin or opium with marijuana or hashish in a joint. (2) smoking PCP.
Ecstasy, *Extacy*	[from the euphoria, heightened sensuality, intensified sexual desire attributed to the drug experience] methylenedioxymethamphetamine (MDMA), a mildly hallucinogenic drug synthesized from methamphetamine and resembling mescaline and LSD in chemical structure
eightball	an eighth of an ounce of cocaine
elephant tranquilizer	PCP
Emilio	[as in Emilio and Maria (Mary), from Mary Jane] marijuana
energize me	give me some crack
equalizer	pebbles of crack cocaine
Eve	[variant of Adam, MDMA, or Ecstasy] MDE, a mild hallucinogen derived from amphetamine. Adam and Eve is a compound of MDMA + MDE = MDEA (*n*-ethyl-MDA or 3, 4, methylene + dioxy-*N*-ethylamphetamine)
Exctasy	Esctasy used with Viragra
Exing	taking Ecstasy
fix	(1) a drug dose needed to hold off withdrawal. (2) a shot of heroin. *See* shoot below.
flake	[from its appearance] (1) cocaine hydrochloride. (2) the sediment of a rock or chunk of cocaine.
Flying Saucers	[tradename] hallucinogenic seeds of a variety of morning glory
forget pill	Rohypnol. *See* roofies below.
freebase	[the psychoactive alkaloid, the base, has been freed or extracted from the cocaine hydrochloride] (1) crystals of pure cocaine. (2) to prepare the base; to smoke it.
frost freak	one who inhales the fumes of Freon, a coolant gas, to get high
funky green luggage	A supply of marijuana in one's baggage
G, *GHB*	gamma-hydroxybutyrate: clear liquid, white powder, tablet, or capsule often combined with alcohol; used mainly by adolescents and young adults, often at nightclubs and raves. GHB is usually abused either for its intoxicating/sedative/euphoriant effects or for its growth hormone-releasing effects which can build muscles.
gangster	marijuana
ganja	[from *gaja*, Hindi word for India's potent marijuana, consisting of the flowering tops and leaves of the hemp plant, where most of the psychoactive resin is concentrated] marijuana
garbage can	drug user who takes anything, everything, combinations
Georgia gamma -hydroxybutyrate	*See* GHB above.
ghost	LSD
girl	cocaine
glass	crystalline methamphetamine
gluey	one who inhales glue forms

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Table 1 (continued). Slang terms. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Term	Definition
goofing	[from *goofballs* = barbiturates, and from *goof*, meaning "to act silly, stupidly, heedlessly"] under the influence of barbiturates
grass	marijuana as chopped up for smoking, looks like dried grass
green	[harvested hemp leaves that are not properly cured; also, the lower leaves of the hemp plant, which contain a smaller proportion of the psychoactive resin] (1) marijuana of low potency, e.g., Chicago green. (2) ketamine, an anesthetic similar to phencyclidine (PCP) but milder in its effects, which is sprinkled on parsley or marijuana and smoked.
grievous bodily harm	gamma-hydroxybutyrate. *See* GHB above.
H	heroin; also Big H
hash, *hashish*	the concentrated resin of the marijuana plant, containing a high percentage of the active principle, tetrahydrocannabinol (THC)
hash oil	liquid extracted from hashish, providing a more potent dose of the active principle and more easily transported in vials. It produces more sedation and deeper states of reverie than hashish,
Henry, *Harry*	heroin
herb	[used to connote a benign natural substance] marijuana
herbal Ecstasy	herbal combinations marketed as a *natural high* that can be legally purchased over the counter in drug stores, music stores, and other shops. The active ingredients include caffeine and ephedrine.
high	[from the sense of euphoria, being above it all, detached from unpleasant reality] intoxicated by a drug
hip	[from lying on the hip to smoke opium— the addict lay on his side on a pad in an opium den; the term was then extended to illicit drug users. In the alienated subculture of the jazz scene of the 1930s and 1940s, using drugs was expected and made one keenly informed or hip (originally *hep*) until *squares* adopted the word] sophisticated, knowing, *in*; possessing taste, knowledge, awareness of the newest trends, and a lifestyle superior to that of conventional people
hit	(1) an injection of a narcotic. (2) a snort of cocaine. (3) a drag from a crack pipe. (4) a toke of marijuana. (5) to adulterate (cut) a drug. (6) a dose of LSD.
hitters	those who inject others who have hard-to-find veins
hog	[from its original use as a veterinary anesthetic] phencyclidine (PCP)
home boy	gamma-hydroxybutyrate. *See* GHB above.
hooch	alcohol
horse	heroin
hot shot	a potent dose of heroin sufficient to kill; heroin laced with cyanide
How do you like me now?	crack cocaine
huff	to inhale ordinary household products to get high. Users huff directly from the container or from inhalant-soaked rags, socks, or rolls of toilet paper. Inhalants include model airplane glue, nail polish remover, cleaning fluids, hair spray, gasoline, the propellant in aerosol whipped cream, spray paint, fabric protector, air conditioner fluid (Freon), cooking spray, and correction fluid.
ice	extremely pure and addictive smokable form of crystalline methamphetamine
J, *jay*	[from *joint*] a marijuana cigarette
jelly babies, *jelly beans*	amphetamine pills
joint	[from *joint* as part of the paraphernalia for injecting narcotics, particularly the needle; since the 1920s] a marijuana cigarette
jonesing	[after John Jones, the British physician who first described opiate withdrawal in 1700] withdrawal from addiction; by extension, craving of any drug
juice	steroids
Julio	marijuana. *See* Emilio and Mary Jane.
junk	[from *junker*, a pusher or peddler; since the 1920s. Also possibly from a word for opium—a play on junk, a Chinese boat—which was later extended to all narcotics] heroin (which is derived from opium)
K, *Super K*, *Special K*, *Vitamin K*	ketamine, an anesthetic similar in structure to PCP. First synthesized by a pharmaceutical company in the early 1960s, powdered ketamine emerged as a recreational drug in the 1970s. It became Vitamin K in the underground club scene in the 1980s and Special K in the 1990s rave scene.
keester plant	[from *keester*, "rump," and *plant*, "to place"] drugs in a rubber container or condom concealed in the rectum
Ketaject, *Ketalar*, *ketamine*	*See* K above.
kick the gong (around)	to smoke opium (especially in a Chinese opium den)
kick the habit	[related to *kick it out*, to suffer withdrawal symptoms, which include muscle spasms in the legs and kicking movements from hyperactive reflexes in the spinal cord] (1) abrupt withdrawal from a drug to which one is addicted. (2) to conquer drug dependence.
kif	marijuana
killer joints	marijuana with PCP
kind buds	potent marijuana. *See* buds above.
LA coke	ketamine. *See* K above.
la roche	Rohypnol. *See* roofies below.
lady	cocaine
laughing gas	nitrous oxide
lid	[from the now obsolete practice of selling a measure of marijuana in a pipe tobacco tin] an ounce of marijuana, usually sold in a plastic bag
line	(1) a thin stream of cocaine on a mirror or other smooth surface, which is sniffed through a quill—a rolled matchbook cover, tube, straw, tightly rolled dollar bill, etc. (2) a measure of cocaine for sale.
liquid Ecstasy	gamma-hydroxybutyrate. *See* GHB above.
luding out	[from *ludes*, short for Quaaludes (brand-name for methaqualone, an addictive sedative)] taking methaqualone
Lyle	[from lysergic acid] LSD
magic mushrooms	hallucinogenic mushrooms
mainline	[from *main line*, a major rail route; since the 1920s] (1) the large vein in the arm; the most accessible vein. (2) to inject morphine, heroin, or cocaine into any vein.
Mary Jane, *MJ*, *Aunt Mary*	marijuana

[CONTINUED]

Table 1 (continued). Slang terms. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Term	Definition
MDMA	Ecstasy
meth	methamphetamine
Mexican brown	marijuana from Mexico
Mexican mud	brown heroin from Mexico. *See* brown above.
microdot	acid
mind-altering	the claimed mental effects of hallucinogenic drugs—altered or intensified states of perception
mind expansion	[related to psychedelic mind-manifesting; a descriptive term for hallucinogenic drugs coined in the 1960s] the claimed mind-altering effects of hallucinogenic drugs, including greater spirituality, enhanced self-awareness, and increased sensitivity to music, art, and nature; also synesthesia & cross-sensations, such as *seeing* music or *hearing* colors
Miss Emma	morphine
monkey on one's back	desperate desire for drugs; addiction; craving
moon	[from the shape of slices of the bud of the peyote cactus] peyote
moonrock	heroin mixed with crack for smoking
Moroccan candy	[*majoun* (Arabic) is candy laced with hashish, sold in Morocco and Afghanistan] hashish. *See* hash above.
mud	heroin
mule	(1) a low-level drug smuggler from Latin America; mules often swallow a condom filled with cocaine to be delivered at a destination—a dangerous practice called bodypacking. (2) heroin.
new Ecstasy	ketamine. *See* K above.
night train	PCP
nose candy	cocaine
on a mission	looking for crack
opium den	[from *den*, an animal's lair. The term was coined by Westerners in 19th-century China, to have lurid connotations] a place where opium is smoked. Chinese laborers brought the practice of smoking opium to America during the gold rush of 1849 and the 1850s. and the building of the transcontinental railroad.
ozone	PCP
pad	[from the mats in opium dens on which the smokers reclined and slept. In the 1930s Harlem apartments where marijuana was sold and smoked while reclining on couches or mattresses were called tea pads] (1) private place for taking drugs; a variant is crashpad, a place for recovering from the effects of a methamphetamine run (period of extended use); the user collapses (crashes) into an exhausted sleep. (2) by extension, since the 1950s, any dwelling place, room, or apartment.
paper bag	a container for drugs
PCP	[from PeaCe Pill] phencyclidine (brand-name Sernyl), a veterinary anesthetic that induces bizarre mental states in humans
peace pill	PCP
pearls	[medical nickname] amyl nitrite ampoules
Persian white	fentanyl. *See* China white above.
p-funk, *p-dope*	[*p* stands for pure] fentanyl. *See* China white above.
PG	paregoric, a traditional diarrhea remedy containing opium
pharming	the consumption of a mixture of drugs
piece	hashish, a form of marijuana. *See* hash above.
piggybacking	either the simultaneous injection of two drugs or the use of more than one tablet of MDMA
pill ladies	female elders who sell OxyContin (Oxycodone)
pill popping	[from popping something into one's mouth] promiscuous use of amphetamine and barbiturate pills or capsules. Drug user who does this is a *popper* and may be a *garbage can*.
pit	veins on the inside of the arm at the elbow, a main site for injecting heroin and the place to look for tracks. *See* ditch above.
pop	to inject. *See* shoot below.
poppers	[the glass ampoule is popped open and the contents inhaled] amyl nitrite ampoules
pot	[from *potaguaya*, a Mexican–Indian word for marijuana] marijuana
psychedelic heroin	ketamine. *See* K above.
pusher	[extension of this definition of *pusher*: a person who circulates counterfeit money; since the 1920s] drug seller, drug dealer. See dealing above
quas, *quacks*	[from Quaalude, brand-name of methaqualone] methaqualone pills, an addictive sedative
Raoul	cocaine
rave	an all-night underground party, usually frequented by teens and college students. Raves are characterized by techno music and often designer drugs, especially Ecstasy.
reds, *red birds*	[also called *red devils*, *red jackets*, *red caps* because of the color of the capsules] Seconal (a brand of secobarbital) capsules
reefer	[from *grifa*, a Mexican–Spanish word for marijuana] (1) a marijuana cigarette. (2) marijuana.
rhoids	steroids
rib	Rohypnol. *See* roofies below.
righteous bush	marijuana plant
ringer	[from the idea of *hearing bells*; *bells* is a term for crack] powerful effect from a hit of crack
roach	[from its resemblance to a cockroach] the butt (end) of a marijuana cigarette
rock	[from its appearance] (1) large crystals or a chunk of pure cocaine hydrochloride. (2) crack. *See* base above.
rocket fuel	PCP
roofies, *rophies*, *ruffies*, *R2*, *roofenol*	Rohypnol, brand-name for the powerful sedative flunitrazepam. The pills are often used in combination with alcohol and other drugs.
rope	Rohypnol. *See* roofies above.
runner	a messenger (often a juvenile) who delivers drugs from the seller to the buyer (not to be confused with a drug runner, a smuggler)
rush	the quick initial onset of orgasmic sensations—of warmth, euphoria, and relaxation after injecting or inhaling heroin, cocaine, or methamphetamine
SAM	a federal narcotics agent
scag	heroin

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Table 1 (continued). Slang terms. ILUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Term	Definition
schoolboy	(1) codeine, a derivative of opium with relatively low potency, used as a cough suppressant and analgesic. (2) morphine.
Scotty	crack cocaine. *See* beamed up above.
script	prescription for a drug, often forged by addicts
script doctor	a physician who will provide a drug prescription for a price, or one who is deceived into providing one
shabu	crystalline methamphetamine
shake	[the mixture is made by shaking the drug and the adulterant] (1) cocaine adulterated (cut) with a harmless substance such as mannitol. (2) loose marijuana left at the bottom of a bag that held a pressed block of marijuana.
sheet	[from decorated blotter paper containing doses of the drug] acid or LSD
shit	heroin
shoot	inject a drug; also shoot up a fix or a shot (usually of heroin)
shooting gallery	place where heroin addicts shoot up and share needles and other drug paraphernalia (*works*)
shoot the breeze	inhale nitrous oxide (called laughing gas).
shrooming	high on hallucinogenic mushrooms
shrooms	hallucinogenic mushrooms
Sid	A play on the *s-d* sound of LSD
sinse	[from sinsemilla, without seeds] a hybrid variety of marijuana; also called *ses*
skin popping	[from *pop*, to inject] injecting heroin or any psychoactive drug subcutaneously (rather than into a vein), a practice of casual (*chippy*) users
skunk	marijuana
smack	[perhaps from *shmek*, Yiddish word for *sniff*, *whiff*, *pinch of snuff*; since the 1910s, when heroin users sniffed the drug; in the 1920s and 1930s some Jewish mobsters were involved in heroin trafficking] heroin
smoke	marijuana
snappers	[the ampoule containing the drug is snapped open] amyl nitrite capsules
snob	[from the idea of an elite or expensive drug] cocaine
snop	marijuana
snort	to sniff a drug
snow	[from its appearance; also, the drug is a topical anesthetic and numbs the mucous membranes] cocaine hydrochloride
snowbirds	cocaine
soapers	[from Sopor, brand-name of a sedative now off the market] methaqualone pills
space basing, space blasting	smoking a mixture of crack and phencyclidine (PCP) speed: (1) amphetamines, (2) caffeine pills, (3) diet pills.
speedball	[first used by GIs during the Korean War] injected mixture of heroin and cocaine
splif	a fat marijuana cigarette
spook	heroin
squirrel	a mixture of PCP and marijuana sprinkled with cocaine and smoked
stash	extension of hobo argot for hiding place; since the 1800s (1) hiding place for drugs. (2) a supply of drugs. (3) to hide drugs.
steerer	member of a cocaine or heroin crew who directs people to the seller
stepped on	adulterated or cut
stick	A marijuana cigarette
street drugs	drugs purchased from sellers on the street; hence, of dubious quality
strung out	severely addicted
sugar cubes	LSD
sunshine	[from the type sold as an orange-colored tablet] LSD
super grass	[the powder is sometimes mixed with parsley or marijuana and smoked] ketamine. *See* green.
tabs	[from *tablet*, a form in which the drug is sold] LSD
tea	marijuana
Thai stick	potent marijuana from Thailand
thing	(1) heroin. (2) an addict's works or hypodermic needle (needle and syringe).
tic	[from THC] fake tetrahydrocannabinol
toke	A drag on a marijuana cigarette
tooies	[from Tuinal, brand-name for a preparation containing amobarbital and secobarbital] sedative capsules
toot	(1) to sniff cocaine. (2) cocaine. (3) a binge, especially a drinking bout or spree (since the late 1700s).
touting	(1) purchasing drugs for someone else. (2) advertising or hawking drugs for sale.
tracks	a line of scabs and scars from frequent intravenous injections. *See* pit and ditch above.
tripping	[from *trip*, in the sense of a psychic journey] taking LSD
trips	(1) LSD tablets. (2) periods under the influence of various drugs, usually hallucinogens.
turkey	[from *turkey*, meaning a "jerk"or "theatrical failure or flop"] (1) a nonpsychoactive substance sold as a drug. (2) the seller of phony substances.
turn on	take drugs, especially hallucinogens
tweak mission	A mission to find crack
ups, uppers	amphetamines
V, Vs	Valium (brand-name for diazepam, a tranquilizer) tablets
wasted	[from *waste*, a street-gang term since the 1950s, meaning "to kill, beat up, destroy"] (1) severely addicted to the point of mental and physical depletion. (2) extremely intoxicated & out of it, beyond caring
weed	marijuana
whack	(1) to adulterate heroin, cocaine, or other drugs. (2) an adulterant. (3) phencyclidine (PCP). (4) to kill
whiff	[from the notion of smelling or sniffing] cocaine
white, white stuff	heroin
white beanies	amphetamines
white lady, white	[from the color] cocaine
window pane	[the drug is sometimes sold in a clear plastic square; also of a greater potency, providing a more intense experience and nonstructured sensations & *opening a window on reality*] LSD

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Table 1 (continued). Slang terms. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Term	Definition
wired	(1) extremely intoxicated by cocaine. (2) anxious and jittery from stimulants (may be related to *amped*, a play on amphetamines and amperes).
woola	[phonetic spelling] a joint containing a mixture of marijuana and crack
works	equipment or paraphernalia for injecting drugs
X, the X, XTC	[from Ecstasy] MDMA
yellow jackets	[from the color of the capsules] Nembutal brand of pentobarbital
yen	[from English slang *yen-yen*, the opium habit, based on Cantonese *in-yan* (*in* meaning "opium" + *yan* meaning "craving"); since the 1800s] any strong craving
zenes	[short for Thorazine, brand-name for chlorpromazine] tranquilizer pills
zombie	(1) crack cocaine. (2) phencyclidine (PCP)
zooted up	high on crack cocaine

Table 1 (continued). Slang terms. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

serve to supplement the reinforcing functions of drug use, making continued drug use more rather than less likely.

According to historical data, the drug trade became popularized in the United States shortly after the end of the Civil War, during the time of national expansion and railroad building, subsequent to the large influx of Chinese laborers, who brought opium with them. With the passage of the Harrison Narcotics Act of 1914, the drug culture was forced to move underground, and addict argot was born. Persons who were opium-dependent were initially called *pipe fiends*; when smoking opium was banned, the term evolved to *dope fiend*. *Yen* came from the Cantonese word used for drug craving, and the phrase *to get one's yen off* referred to doing whatever was necessary to eliminate the symptoms of withdrawal among those who suddenly found themselves without ready access to drugs. *Yen-hock* was a large needle used to prepare opium for smoking, and *yenshee* was the residue left in the bowl after opium was smoked. Opium caused intestinal difficulties and often resulted in constipation, and a *yenshee baby* was a slang term for a particularly painful bowel movement subsequent to the smoking of opium.

Other general slang terms were *hop-head*, *gowster*, *user*, *gow-head*, *smacker*, *cookie*, *user*, *yenshee quay*, and *dope-hop*. In the 1920s *junker* became a universal term for a drug abuser. As the use of intravenously injected drugs grew in popularity, the side effects of this (local skin irritation) became well-known, and the term *laughing and scratching* became jargon for intravenous (IV) drug use. Those who continued to smoke opium were said to be *kicking the gong around* or *laying on the hip*. In the 1930s the term *high* was coined to describe a state of intoxication brought on by the excessive use of drugs. Synonymous with high were *geed up*, *polluted*, *full of poison*, *loaded*, and *leaping*. The needle and syringe used in IV drug administration were referred to as a *harpoon*, a *nail*, a *spike*, or a *point*. Illicit drugs, in general, were referred to as *smack*, *junk*, *stuff*, and *hocus*, among others. By the mid-1930s specific slang developed for various drugs: Heroin was referred to as *H* and morphine as *M*, and very pure drugs, particularly with reference to heroin, were called *the real McCoys*. Individuals who used drugs very frequently were said to be *mainliners*, which came to specifically describe those who used drugs intravenously. Occasional drug users were said to have a *weekend habit*, *chippy-habit*, or *ice-cream habit*. People experiencing drug withdrawal without any assistance or intervention were said to be *going cold turkey*, apparently as a result of their pale bumpy skin brought on by the chills of withdrawal, or *kicking the habit*. The *iron cure* was forced withdrawal in a jail or prison setting.

Slang terms in the drug subculture are constantly changing, as its ethnic, social, and demographic composition changes and as new illicit drugs roll in and roll out with the tides of fashion, including geographical variations. Certain terms nevertheless show a remarkable durability, such as some of those used for heroin (first marketed by the German pharmaceutical concern, Bayer, in 1898), a narcotic that has been a staple street anodyne since the early 1900s. Drug-related terms that originated within the drug culture of the early twentieth century have come into the mainstream, remaining a permanent part of the English language, for example, *yen*, *hooked*, *pad*, *spaced out*, *high*, and *hip*. *Dope* has become a

general-purpose term, widely used in relation to numerous types of drug; many people know that *weed* or *reefer* refers to marijuana, whereas *acid* is lysergic acid diethylamide or LSD.

Table 1 lists many words that came into common use during much of the twentieth century (a few antiques of sociological or historical interest are included, too). Some terms are the product of the 1980s and 1990s. Origins, if known, are given.

See also **Cocaine; Epidemics of Drug Abuse in the United States; Heroin; Marijuana (Cannabis); Opium: U.S. Overview.**

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SLEEP, DREAMING, AND DRUGS.

The use of psychoactive drugs and alcohol to hasten the onset of sleep and to enhance the experience of dreaming is a phenomenon that dates to prehistory. The ancient Greeks used hallucinatory substances for religious purposes. The priestesses at Delphi, for example, chewed certain leaves while sitting in a smoke-filled chamber and going into a trance. On returning to consciousness, they would bring forth a divine prophecy. The various Dionysian cults encouraged their celebrants to enter ecstatic dream-like states through the use of wine and perhaps other drugs. The ancient Hindus imbibed a sacred drink called *soma*, and marijuana was used in practices of

meditation. For the Arabs, hashish (a form of marijuana) was the substance of choice, while the Incas chewed the leaves of the coca plant (from which cocaine may be made). The opium poppy was used in Asia, and the ancient Mexicans used a variety of powerful psychoactive substances, including peyote, sacred mushrooms, and seeds from the Mexican morning glory plant, to enter the realm of dreams. The Australian aboriginals used the *pituri*, a psychoactive substance, to take them into "dream time," as they referred to it.

ALCOHOL

The effects of ethanol (alcohol) on sleep are complex and somewhat paradoxical. The acute bedtime administration of ethanol to healthy, nonalcoholic volunteers shortens the latency to sleep onset and, depending on dose, may initially increase the amount of relaxed, deep slow-wave (delta-wave) sleep. Additionally, ethanol reduces the amount of REM sleep, usually affecting the second REM period. An ethanol concentration in the blood of 50-milligram percent (mg%) or greater (80 mg% is legal intoxication in all states) is necessary to observe these sleep effects. The sleep effects of ethanol are observed primarily during the first half of an eight-hour sleep period. Ethanol is metabolized at a constant rate, and consequently the usual dose of ethanol (resulting in a blood alcohol concentration of 50–90 mg%) given in these studies is almost completely eliminated from the body after four or five hours.

Following elimination of ethanol, an apparent compensatory effect on sleep occurs. During the latter half of sleep, increased amounts of REM sleep and increased wakefulness or light sleep are found. Within three to four nights of repeated administration of the same dose of ethanol, tolerance occurs, and the initial effects on sleep are lost, while the secondary disruption of sleep during the latter half of the night persists. REM sleep time and sleep latency return to their basal levels, and the effects on slow-wave sleep, when initially present, do not persist. When nightly administration of ethanol is discontinued, a REM rebound is seen. But the REM rebound after repeated nightly ethanol administration in healthy, nonalcoholic subjects is neither consistent nor predictable. In alcoholics, however, the REM rebound has been demonstrated to be both intense and persistent. Some believe the presence of a REM rebound is characteristic of drugs with a high addictive potential.

OPIATES

Belladonna and opiates have historically been used for the specific purpose of producing vivid dreams. The most famous illustration is the story of the English poet Samuel Taylor Coleridge (1772–1834), who allegedly wrote his most celebrated work, "Kubla Khan," during a drug-induced dream. Lysergic acid diethylamide (LSD) became popular in the United States and Europe during the 1960s for allegedly facilitating higher states of consciousness and creativity. The writer John Lilley used a sensory-deprivation tank to emulate the state of sleep while taking LSD to induce creative dreaming.

Reference to the effects of drugs and alcohol on sleep and dreaming are also found in popular literature. It was a mixture made from poppies that caused Dorothy and her companions to fall into deep sleep in the *Wizard of Oz*. After ingesting a series of pills and liquids, in *Through the Looking Glass*, Alice finds herself in "Wonderland," where she has a conversation with an opium-smoking caterpillar who is sitting on a magic mushroom that alters the state of one who eats of it. After returning to the reality of her home in England, Alice realizes that she had, of course, fallen asleep and been dreaming.

Modern study of the effects of drugs and alcohol on sleep and dreams dates to the mid-1950s. With the use of electrophysiological machines, including electroencephalograms (EEGs), electrooculograms, and electromyograms, the state of sleep most closely associated with dreaming was discovered, studied, and named REM, for the rapid eye movements unique to that sleep state. In humans, REM sleep recurs in approximately 90-minute cycles throughout the sleep period, resulting in four or five REM episodes per night, each lasting from 10 to 30 minutes. Adults spend about 20 to 25 percent of their sleep period in REM sleep. Abrupt awakening from REM sleep is consistently associated with the recall of vivid dreaming. While the function of REM sleep is not completely understood, it appears to serve a necessary function. Deprivation of REM sleep by awakenings or by the administration of REM-suppressing drugs leads to a compensatory or rebound effect, specifically, a more rapid onset

and a greater amount and intensity of REM sleep, when the sleep pattern is able to return to normal. This indicates that there is a physiological need for REM sleep, as deprivation of it causes an accumulation of need that must be satisfied for baseline sleep patterns to resume.

Many psychoactive substances have meaningful effects on sleep and particularly on REM sleep. While the effects of drugs on REM sleep are known, their effects on dreaming continue to be studied. Given the association of REM sleep and dreaming, one might think that REM-enhancing drugs would increase dreaming, while REM-suppressing drugs would decrease dreaming. The existing data as of 2008 suggest that the relationship is not that simple. After the discontinuation of REM-suppressing drugs, a REM rebound occurs, which is reported to be associated with increased and unpleasant dreams, as well as nightmares. Some have hypothesized that the visual hallucinations experienced during discontinuation of some drugs (e.g., alcohol) is a REM rebound intruding into wakefulness. While it is reductive to think of dreaming and REM in a one-to-one correspondence, it is reasonable to assume that drugs affecting REM will also affect the frequency and nature of dreams.

Morphine and Heroin. Morphine, an opiate analgesic (derived from the opium poppy), decreases the number and the duration of REM sleep episodes and delays the onset of the first REM period. It also increases awakenings and light sleep and suppresses slow-wave sleep. Heroin, a semi-synthetic opiate, also suppresses REM sleep and slow-wave sleep and increases wakefulness and light sleep, producing a disruption of the usual continuity of sleep. Heroin appears to be more potent than morphine in its sleep effects. The synthetic opiate, methadone, has similar effects on sleep and wakefulness, with a potency more comparable to that of morphine. When an opiate is administered just before the onset of sleep, the EEG pattern shows isolated bursts of delta waves on the background of a waking pattern. Animal studies have correlated these delta bursts with the behavior of head nodding (a possible physiological correlate to the street term *being on the nod*). Repeated administration of the opiates at the same dose leads to tolerance to the sleep effects of these drugs, particularly the REM sleep effects. The cessation of opiate use leads to a protracted REM rebound, increased REM sleep, and a shortened latency to the first REM episode.

STIMULANTS

Stimulants, including amphetamines, when administered before sleep, delay sleep onset, increase wakefulness during the sleep period, and specifically suppress REM sleep. Cessation of chronic amphetamine use is associated with an increase in slow-wave sleep on the first recovery night and, on subsequent nights, with increased amounts of REM sleep and a reduced latency to the first episode of REM sleep, i.e., REM rebound.

Caffeine interferes with sleep in most nontolerant individuals. Once tolerance has developed, people are much less likely to report sleep disturbances, or they may sense that their inability to sleep because of caffeine intake has completely disappeared. To illustrate, 53 percent of those consuming less than 250 mg per day (about 2 to 3 cups of coffee) agreed that caffeine before bedtime would prevent sleep, compared to 43 percent of those consuming 250 to 749 mg per day, and only 22 percent of those consuming 750 mg per day or more. Even though the higher level caffeine consumers denied that caffeine interferes with their sleep, studies done in sleep laboratories confirm that caffeine consumers do have greater sleep latency, more frequent awakenings, and altered sleep architecture, and that these effects are dose-related. One study that investigated the effects of day-long consumption of coffee and tea on sleep onset and sleep quality demonstrated that caffeinated beverages had a dose-dependent negative effect on sleep onset, sleep time, and sleep quality.

Nicotine. Nicotine has varying effects on sleep. In a study conducted in rats, the higher the dose of nicotine that was administered, the lower the tota sleep time. In a study of the effects of nicotine transdermal patches on depressed patients, nicotine increased REM sleep time and alleviated some symptoms of depression. But another study that assessed the effects on sleep of four different doses of 24-hour transdermal nicotine showed no changes in sleep efficiency from baseline for any of the doses used. When a person is attempting to withdraw from nicotine addiction, sleep and concentration difficulties are often reported. Research has demonstrated that

such withdrawal symptoms are lessened by maintaining an adequate blood level of nicotine, as can be supplied by transdermal patches. In that setting, sleep can appear to be enhanced by the use of 24-hour nicotine patches.

Cocaine. Cocaine also has stimulant effects on the central nervous system. Cocaine's effects on electroencephalogram readings were first studied in 1931 by Hans Berger (1873–1941), the Swiss researcher who developed the EEG. Cocaine was found to increase fast-frequency EEG activity, suggesting an alerting effect. The self-reported use of cocaine during the late afternoon and early evening is associated with reduced nocturnal sleep time. Electrophysiological studies show a reduction of REM sleep following cocaine administration. Cessation of chronic cocaine abuse is followed by increased sleep time and a REM rebound.

HALLUCINOGENS

The three classic hallucinogens are LSD, mescaline, and psilocybin. The state experienced following use of hallucinogens is somewhat similar to dreaming. Since REM sleep is highly correlated with dreaming, it would be expected that the hallucinogens facilitate REM sleep, but LSD is the only hallucinogen as of 2008 that has been systematically studied for its effects on sleep. One study done in humans showed that LSD enhanced REM sleep early in the night, although it did not alter the total amount of REM sleep for the night. However, studies in animals all indicate that LSD increases wakefulness and decreases the first episode of REM sleep for the night. The brain wave frequency changes seen in the waking EEG of animals (similar among all three hallucinogens) suggest an arousing effect. Thus the REM suppression seen with hallucinogen administration in animals may not be a specific REM effect but rather a sleep-suppressing effect.

Marijuana. Another drug with some hallucinogenic effects is marijuana, its active ingredient being tetrahydrocannabinol (THC). The effects of THC on the waking EEG pattern are significantly different than the effects of the classic hallucinogens cited above. THC has sedating effects at lower doses and hallucinatory effects at higher doses. The acute administration of marijuana or THC to humans is associated with an increase in slow-wave sleep and a reduction in REM sleep. When THC is administered chronically (long-term), the effects on slow-wave and REM sleep diminish, indicating the presence of tolerance. Discontinuing the use of marijuana is associated with temporarily increased wakefulness and increased REM sleep time.

Most of these drugs, which are also drugs of abuse, have some effects on sleep, particularly on the amount and timing of REM sleep. Each affects chemicals in the brain that control sleep and wakefulness and, with chronic use, some adaptation is typically reported to occur. A characteristic REM rebound is seen on discontinuation of protracted drug use. (It may be that the ancients' experience of enhanced dreaming was the REM rebound that is typically associated with protracted drug use.) Some studies indicate that, in the formerly drug dependent individuals in recovery, the occurrence and intensity of the REM rebound has been predictive of relapse to drug use. How the sleep-wake pattern changes—and specifically the REM changes associated with these drugs— contribute to their excessive use need further study.

See also **Addiction: Concepts and Definitions; Benzodiazepines: Complications; Sedative-Hypnotic; Sedatives: Adverse Consequences of Chronic Use; Tolerance and Physical Dependence.**

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SLEEPING PILLS. This is a general term applied to a number of different drugs in pill form that help induce sleep, i.e. sedative-hypnotic agents. There is a wide range of such medications. Many require a doctor's prescription, but some can be purchased as over-the-counter drugs at a pharmacy. These latter preparations generally contain an antihistamine such as chlorpheniramine maleate, which produces drowsiness.

The prescription medications are much stronger. They include barbiturates, benzodiazepines, and a number of other compounds. However, due to the risk for fatal overdose, especially in combination with alcohol or other CNS depressants, the barbiturates are no longer widely prescribed for this indication. In general, the shorter-acting sleeping pills are used to help one relax enough to get to sleep, while the longer-acting ones are used to help prevent frequent awakenings during the night. Long-term or inappropriate use can lead to tolerance and physical dependence.

See also **Sedative-Hypnotic; Sedatives: Adverse Consequences of Chronic Use.**

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SMART RECOVERY AND RATIONAL RECOVERY. Self-Management and Response Training (SMART) Recovery was formerly named the Rational Recovery Self-Help Network, and it was affiliated with the Rational Recovery (RR) program founded by Jack and Lois Trimpey. After a series of disagreements between Mr. Trimpey and the board of directors overseeing the Self-Help Network concerning the programs to be offered by the self-help groups, there was a mutual parting of the ways. In 1994, the Self-Help Network changed its name to SMART Recovery and severed its affiliation with RR.

The main difference between the two programs has to do with governance. A board of directors oversees SMART, a not-for-profit corporation (501c3), and RR, a for-profit corporation, is owned exclusively by the Trimpeys. There are some philosophical differences as well. RR appears to focus primarily on coping with urges, whereas SMART includes attention to motivation, controlling urges, problem-solving, and leading a balanced life. It is based on scientific knowledge and good practice as interpreted by the board of directors and the program committee. The conceptual framework for SMART Recovery is based on the principles of Rational Emotive Behavior Theory, as espoused by Albert Ellis and E. Velten (1992).

SMART Recovery is an evidence-based program utilizing groups, online meetings, online chat, and face-to-face meetings to assist people in recovery from the continuum of addictive behaviors, including (but not limited to) alcoholism, illicit drug abuse in general, general abuse of prescription medications, gambling and sex addiction, cocaine addiction, eating disorders, and addiction to other unwanted behaviors or substances. All programs are offered free of charge, although donations are accepted. SMART Recovery is offered as an alternative to the more traditional, spiritually based twelve-step groups. In

an average week, SMART sponsors more than 300 face-to-face meetings worldwide, as well as nearly 20 online meetings. There is also an extensive interactive Web site and a message board.

SMART Recovery's stated mission is to assist and support individuals who are striving to achieve and sustain abstinence by offering a variety of educational opportunities, tools, and techniques as mechanisms for behavior change to help them shift from self-defeating thinking, emotions, and actions and achieve a lifestyle that brings both internal satisfaction and an improved quality of life.

SMART Recovery is based on a four-point program:

1. Enhancing and maintaining motivation to abstain.
2. Coping with urges.
3. Problem-solving: managing thoughts, feelings and behaviors.
4. Lifestyle balance: balancing momentary and enduring satisfactions.

The SMART Recovery program focuses on empowering individuals to free themselves from addictions and unwanted behaviors. There are myriad tools and techniques incorporated into the four-point program, with the understanding that they need repetition and practice to attain mastery. Skill building is progressive over time and across the four points.

RATIONAL RECOVERY

Jack and Lois Trimpey started Rational Recovery in 1986. It is focused on addiction recovery through abstinence and states that it is the "antithesis and irreconcilable arch-rival of Alcoholics Anonymous." RR purports that addiction is a choice, not a disease manifestation; co-dependency does not exist; and that group meetings can lead to substitute addiction and are, at best, counterproductive. RR holds that recovery from addiction is a highly personal journey that can best occur without external sources of support (groups, sponsors, family, friends, medical personnel, etc.). It also holds that people become addicts not because of genetic predisposition, cultural factors, poverty, stress, self-medication, or low self-esteem but simply because it feels good to be high.

A cornerstone of RR is Addictive Voice Recognition Technique (AVRT). This technique is based on the belief that the urge to use addicting substances arises from the primitive brain, which is based on instinctive, irrational, animal urges to seek pleasure. By recognizing this and giving it a name, the Addictive Voice (AV), it is possible to overcome it and conquer addictions. The AV becomes separated from the rest of the self through the use of the RR principles, and "*I* want to get high" becomes "*It* wants to get high." By shifting to thoughts of power and control to overcome the AV, recovery becomes automatic and, in RR parlance, effortless. *Never* is the operative word for abstinence, and living in the moment is key, so "I will never use drugs again" shifts to "I never use drugs now." The *Crash Course on AVRT*, which teaches abstinence techniques, is available on the Rational Recovery Web site.

Because neither program is able to collect complete outcome data, the overall effectiveness of SMART Recovery and of Rational Recovery is unknown. There are no reliable or valid outcome data for *any* self-help program, because of both the policy of anonymity that is a cornerstone of self-help programs and the relative scientific informality of such groups.

See also **Alcoholics Anonymous (AA); Sobriety; Treatment, Behavioral Approaches to: Self-Help and Anonymous Groups.**

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SOBRIETY. The term *sobriety* is not defined in current medical or psychiatric literature. The term *abstinence* is found more often and is generally agreed upon as the treatment goal for severe alcoholics. Abstinence is defined as nonuse of the substance to which a person was addicted.

SOBRIETY AND SUBSTANCE ABUSE

The term *sobriety* is used by members of Alcoholics Anonymous (AA) and Narcotics Anonymous (NA), and also by members of other Twelve-Step groups and recovery groups not affiliated with AA. In AA and NA, sobriety is often preceded by the adjectives "stable" or "serene." Abstinence—the condition of being sober—is a necessary but insufficient condition for sobriety. Sobriety means something different from the *initial* abstinence so often achieved by alcoholics and other drug addicts. This initial abstinence is recognized as a time of vulnerability to RELAPSE, often referred to as a "dry drunk" or "white-knuckle sobriety."

Sobriety in NA and AA. According to AA beliefs, recovery from alcoholism and other addictions calls for more than just abstinence. The addict's central nervous system must undergo a substantial readaptation. This requirement means that the craving, drug-seeking, dysphoria (unhappiness), and negative cognitions that characterize early abstinence must not only diminish but must also be replaced by more normal positive behavior. This readaptation requires time and substitute activities. The activities most associated with successful readaptation are found in treatment programs and in AA or NA.

Sobriety, as used by most recovering people in AA and NA, refers to abstinence plus a program of activity designed to make the abstinence comfortable and to improve functioning in relationships and in other aspects of life. The program of recovery that leads to stable sobriety usually includes: (1) attending AA and/or NA meetings; (2) "working" the Twelve Steps and continuing to use steps 10, 11, and 12 for the maintenance of sobriety; (3) working with a sponsor who acts as a mentor in maintaining sobriety; (4) belonging to a home group and engaging in service activities that help others with their sobriety; and (5) other activities that enhance or support sobriety (e.g., exercise, hobbies, and psychotherapy). A program of recovery recognizes that any activity has potential to either enhance or interfere with the recovering individual's sobriety. In addition, Twelve-Step programs emphasize the importance of basing sobriety on positive beliefs and ideals. "Shotgun sobriety" is defined in AA as a type of sobriety based only on fear of drinking.

Sobriety in Non-AA Recovery Groups. Secular Organization for Sobriety (SOS), Women for Sobriety (WFS), LifeRing Secular Recovery (LSR), and similar recovery groups for substance abusers also define sobriety in terms of abstinence from drugs and alcohol. A LifeRing pamphlet states, "Please look elsewhere for support if your intention is to keep drinking or using, but not so much, or to stop drinking but continue using, or stop using but continue drinking. The successful LifeRing participant practices the Sobriety Priority, meaning that nothing is allowed to interfere with staying abstinent from alcohol and drugs."

SOBRIETY AND BEHAVIORAL ADDICTIONS

One complication of the term *sobriety* has been the difficulty of defining it in the context of the so-called "process addictions" or "behavioral addictions," terms that have been used to distinguish addictions to such activities or behaviors as gambling, shopping, overeating, sexual acting-out, etc. from substance addictions in the strict sense. Unlike alcoholics and drug abusers, people with behavioral addictions cannot always define sobriety as simple abstinence. A compulsive overeater, for example, must learn to consume food in moderation, not avoid it. Persons addicted to compulsive spending or shopping cannot simply abstain from making purchases. Members of Sex Addicts Anonymous (SAA) rarely define sexual sobriety as complete abstinence from sex, although at times recovering persons may practice complete abstinence (celibacy) for a period of time in order to gain perspective on their life. In this Twelve-Step

group, sexual sobriety is most often defined as "a contract that the sexual addict makes between him/herself and their 12-step recovery support and/or their therapist/clergy. These contracts . . . are always written and involve clearly defined concrete behaviors from which the sexual addict has committed to abstain in order to define their sobriety." Comparable abstinence contracts are used by recovering binge eaters, compulsive spenders, relationship addicts, etc.

One benefit of attempts to redefine sobriety in the context of behavioral addictions is that they have called attention to the problem of substitute addictions, which are addictions that develop when a recovering alcoholic or drug abuser substitutes food, tobacco, or certain activities (including exercise) for their drug of choice. Many members of Twelve-Step groups have found that sobriety requires a reexamination of addictive beliefs and attitudes in general as well as abstinence from alcohol or specific drugs.

SPONTANEOUS RECOVERY

One question that has arisen in recent years is whether some alcoholics can achieve sobriety through spontaneous recovery. G. G. May (1988) uses the term *deliverance* for this phenomenon and defines it as "healing [that] takes the form of empowerment that enables people to modify addictive behavior." Some researchers suggest that spontaneous remission and recovery is more common among alcoholics than was once believed, and that it is connected to growth and maturity in the course of the adult life cycle. G. E. Vaillant (1983) found that most alcoholics in his study outgrew their drinking problem, more often than not without going into treatment or joining AA. Stanton Peele (1992) is perhaps the best-known proponent of the view that "... some people who appear completely out of control of their actions at one point significantly change their outlooks and ability to regulate their behavior later in life." He likens spontaneous recovery of sobriety to the ability of some smokers to suddenly quit using tobacco.

SOBRIETY: SUMMARY

Despite these problems of precise definition, the concept of sobriety (abstinence or its equivalent for nonchemical addictions, plus a program of activity designed to make abstinence comfortable) is a useful one for health care professionals.

See also **Addiction: Concepts and Definitions; Treatment, Behavioral Approaches to: Minnesota Model; Treatment, Behavioral Approaches to: Self-Help and Anonymous Groups.**

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SOCIAL COSTS OF ALCOHOL AND DRUG ABUSE.

Drinking, smoking, and the use of psychotropic drugs have a variety of consequences for those who use them, for their families and associates, and for society at large. A number of these consequences are negative. Smokers can die

young from heart or lung disease, drinkers can get into traffic accidents and fights, drug injectors can spread the HIV virus. In the context of public policymaking, when priorities must be set for the use of scarce resources, it seems important to have a measure of the overall magnitude of the social burden engendered by such consequences. One familiar approach is to express the magnitude of the problem in terms of the number of people who die each year. When one learns that there are over 50,000 deaths per year in the United States from alcohol abuse (National Highway Transportation Safety Administration, 2006), almost 20,000 from drug abuse other than alcohol (Centers for Disease Control, 2007), and that between 1.2 and 1.6 million Americans visited emergency rooms for situations associated with drug misuse or abuse (Substance Abuse and Mental Health Services Administration, 2007), it becomes clear that the stakes are very high in devising sound policies for controlling drinking and drugging. Such statistics, compelling as they are, tell only part of the story. In addition to causing early death, substance abuse makes for a variety of consequences that reduce the quality of life both for users and for other people.

To capture this broad array of consequences in a single number, analysts have estimated various measures of social cost. The estimates are important because they figure in the political process by which federal funds are allocated to the National Institutes of Health (NIH), the Substance Abuse and Mental Health Services Administration (SAMHSA) and to other agencies that play a role in combating substance abuse. A conceptual apparatus developed by a task force of the U.S. Public Health Service chaired by Dorothy Rice (Hodgson & Meiners, 1979) has been used to derive the most prominent estimates of social costs for substance abuse. In 1994 the International Symposium on the Economic and Social Costs of Substance Abuse issued guidelines recommending the use of this cost-of-illness (COI) method in an attempt to establish a common foundation and enhance the comparability of cost studies conducted in different countries (International Center for Alcohol Policies [ICAP], 1999).

Although prominent in policy debate, the cost-of-illness (COI) method has been faulted for its emphasis on production as the measure of social welfare. Economists favor a quite different approach that measures social welfare from the perspective of the consumer. The economists' preferred accounting framework is referred to in this entry as the *external social-cost* approach.

THE TWO FRAMEWORKS APPLIED TO SUBSTANCE ABUSE

A coherent assessment of the social costs of substance abuse requires an accounting framework that specifies criteria for judging which of the myriad effects are deemed to be of public concern. For example, in the case of drinking, on any one drinking occasion there may be harmful consequences: social embarrassment, loss of reputation or affection, failure to discharge some responsibility at work or home, physical injury from an accident, victimization by a mugger or rapist, and nausea or hangover. Chronic heavy drinking may result in still other consequences including rejection by family and friends, loss of a job or of an opportunity for promotion, progressive deterioration in physical health, and an early death. To capture these and other negative consequences in a single number, the list of consequences must be reviewed to determine which should be considered in establishing priorities for substance abuse policy. The consequences deemed relevant must then be quantified, translated into a standard unit of account (dollars), and summed.

The Cost-of-Illness Framework. The COI approach is concerned with measuring the loss or diversion of productive resources resulting from an illness or activity. In the case of alcohol abuse, human capital resources are lost and the gross national product reduced by the morbidity and early death of some drinkers, whether because of injuries sustained in alcohol-related traffic accidents or violent crime or because of organ damage and other diseases stemming from chronic heavy drinking. The loss to society in these cases is equal to the loss of the marginal product of the victims' labor, valued at the market wage. Unpaid work at home, including housework and child care, is included in the computation with values being assigned according to how much households pay for such services when paid employees are hired to do the work.

The COI approach also takes account of the diversion of resources from other productive uses

necessitated by alcohol abuse. Thus the costs of medical care for alcohol-related illness and drug-related illness, treatment for alcoholism and drug abuse, and research on prevention and treatment are incorporated in the social-cost estimate. Similarly, the value of law-enforcement and justice resources devoted to alcohol-related crimes are included as are the costs of replacing property damaged in traffic accidents and fires caused by drinking.

Several prominent estimates of the total costs of alcohol abuse for the United States have used the COI framework (Berry & Boland, 1977; Harwood et al., 1998). In 1998 H. J. Harwood et al. published the most complete COI study to date, and using figures from 1992, the most recent year for which complete data were available, they found that the economic costs to society of alcohol abuse totaled $148 billion, broken down as follows:

About three quarters ($107 billion) of the total cost in this tabulation is the value of labor productivity lost because of illness, injury, or early death. The human capital lost because of alcohol-related mortality was computed for all those who died in 1992 from causes in which intoxication or chronic heavy drinking played a role. These include traffic fatalities and deaths from liver cirrhosis among other causes. The lost human capital was valued by estimating how much the deceased would have earned if they had lived and worked until retirement age;

The human capital lost because of morbidity was calculated by estimating the reduction in the productivity of the labor force resulting from alcohol dependence or abuse. Harwood et al. combined two sets of estimates to arrive at this number: (a) the percentage of the labor force in 1992 that was or had ever been subject to a diagnosis of alcohol dependence or abuse, and (b) an estimate of the loss in earnings associated with such a diagnosis.

Estimates of this sort have been challenged for two reasons. The first challenge is to the statistical methods used to generate the estimates of morbidity, mortality, and lost earnings (Cook, 1991). The second challenge is more fundamental because it concerns the basic principles that inform the COI accounting framework.

The COI procedure estimates the costs of morbidity and mortality in terms of lost productivity, but this emphasis on production as the measure of social welfare seems misplaced. A more liberal perspective, favored by economists among others, shifts the emphasis to consumption and interprets the task of measuring social welfare in terms of aggregating individual preferences. People are the best judges of their own welfare. It should not be considered problematic if sometimes they make choices that fail to maximize their productivity. In this view the choices that people make concerning how hard to work and when to retire are of little public concern. The same goes for choices that place someone's own health and safety at risk. Thus in economics there is a strong presumption in favor of consumer sovereignty, the principle that the individual person is in the best position to define what is best for him or her, and that social welfare is enhanced by free choice within certain limits. A negative consequence is deemed to be of *public* concern only when the actions of one individual impinge negatively on the welfare of others. The basic distinction, then, is between *internal* and *external* consequences of individual decisions, where the latter impose an involuntary cost on other people.

In the case of alcohol abuse, the internal costs include those suffered by drinkers and are foreseeable as a natural consequence of their choices. A small example explains the reasoning here. Suppose a woman decides to drink heavily despite knowing that she may be tired and unproductive the next day. By making this decision she is indicating that for her the pleasure of drinking outweighs the morning-after costs. The external costs are zero if no one else is harmed by this decision. If she were to drive after drinking, however, the accounting would change. She would be risking serious injury to herself and to others on the highway. Her injury would have external costs to the extent that a third party (group insurance or Medicaid) paid her medical expenses, and the risk that she might injure other people while driving is to be valued at the expected loss to them. That cost is not limited to their lost earnings but also includes their pain and suffering and the suffering of those who care about them.

The most fundamental challenge to the COI framework relates to its presumption that social

welfare is synonymous with national product. Economists argue instead that the preferences of individuals are the proper measure of their well-being and that social welfare is the sum total of individual welfare. Some of the major costs in the COI framework, especially lost earnings, are less important in the external social-cost view, whereas a number of costs that are ignored in COI become important when the focus is on external costs.

The External Social-Cost Framework. In a study at the Rand Corporation, economists applied the external social-cost (ESC) framework to alcohol abuse and other poor health habits (Manning et al., 1989, 1991). Their estimate for alcohol abuse amounted to about $30 billion in 1985, less than half the COI estimate presented above for the same year. The accounting procedures used to generate this estimate of the ESC can be briefly summarized:

- Heavy drinkers might have earned less than they otherwise would have during their careers and might have had their careers cut short by poor health and early death. Although the most obvious effect was a reduced standard of living, which was considered a private cost, a number of programs created a collective interest in the productivity of each individual. For example, those who died young saved their fellow citizens the expense of years of pension payments and medical costs. Those who retired early (perhaps because of poor health) imposed financial costs on others because their contributions to the Social Security system were reduced. Thus these collective financing arrangements had the effect of creating both external costs and external benefits in relation to heavy drinking. The net effect, according to W. G. Manning et al. (1991), was negative and equaled about 22 percent of the total external cost;
- Heien (1996) reported that about 3,765 of the 13,984 people who died in alcohol-related traffic accidents in 1993 were innocent because they had not been drinking at the time. Their lives had value not because their work increased the size of the national product but because they enjoyed life. People are willing to pay to reduce the risk of a fatal accident, and the social cost of these innocent deaths is in principle equal to the total amount the public would be willing to pay to eliminate the threat of being killed by a drunk driver. Manning et al. (1991) employed this willingness-to-pay approach and found that nearly half of the social cost of alcohol abuse stemmed from traffic fatalities;
- The remaining $7.2 billion in the Manning et al. (1991) social-cost estimate stemmed primarily from the burden of alcohol-related cases on the criminal justice system and the share of collision insurance costs accounted for by the property damage caused by drunk drivers.

It appears that in several respects these estimates are incomplete. The costs of alcohol-related injuries to innocent victims are far higher than indicated by Manning et al. because they omitted the financial and personal costs of nonfatal injuries in traffic accidents (Miller & Blincoe, 1993) and the costs of both fatal and nonfatal injuries from violent crimes perpetrated by drunks. In addition, recent research has suggested that moderate alcohol consumption carries measurable health benefits, which must also be figured into any equation attempting to assess social costs (ICAP, 1999).

An even more interesting controversy has surfaced over the basic perspective that informs these external social-cost estimates. Some critics reject outright the liberal doctrine that individual preferences are to be accorded primacy in the definition of social welfare and social cost. They postulate a collective interest that can somehow be defined without reference to the choices made by individuals (Beauchamp, 1980). The COI approach reflects one such definition. Other critics accept the liberal doctrine but argue about its application. A particularly difficult set of philosophical and practical issues arises in setting the boundary between internal and external costs in the context of the family. Manning et al. (1991) view the family as a unit and accept the presumption that each member of the family will internalize the concerns of the others and act accordingly. In 1992 Harwood et al. found that abusers and their households bore $66.8 billion of the total cost of alcohol abuse. If the father is a heavy drinker or smoker it is not because he is unaware or unconcerned about the consequences for his wife and children, but because his enjoyment of these activities

outweighs the costs to them. That presumption may seem particularly problematic in the case where the mother's substance abuse causes her baby to have birth defects.

COSTS OF DRUG USE AND ALCOHOL ABUSE

In calculating the current estimated social costs of alcohol abuse and drug use, analysts are forced to rely on data that may or may not have been developed consistent with one of the two approaches described above. Cost attributions for illegal drug use include but are not limited to: treatment and rehabilitation; emergency room consequences; lost productivity; increased demand for social services provided to dysfunctional families because of such use including the consequences of family violence, deaths from drug-related vehicle accidents (drugged driving), and drug-related illnesses; and law enforcement costs that are shifted from traditional activities to responding to the rise of local clandestine methamphetamine labs, drug use in schools, and related activities.

The most recent comprehensive assessment of the social costs of illegal drug use occurred in 2001 when the White House Office of National Drug Control Policy published a study on the social costs of drug abuse that indicated overall costs in excess of $160 billion a year (Office of National Drug Control Policy, 2001).

As the introduction in the 2001 study notes:

> The most recent previous estimates of drug abuse related costs are for 1995 as developed by Harwood et al. (1998). In addition to providing new estimates of the societal cost of drug abuse, this report provides annual estimates for 1992 through 1998 and projections for 1999 and 2000 that are consistently developed so that trends in the overall societal cost and in component costs of drug abuse can be evaluated. Projections are only provided for 1999 and 2000 because there is a significant lag in the availability of the base data for estimating the component values. For the majority of components the most recent data available is from 1998. The estimates have followed guidelines developed by the U.S. Public Health Service for cost-of-illness studies. These guidelines have been applied in earlier studies of drug abuse in the U.S. (e.g., for 1992, 1985, 1980, and 1977), and to cost-of-illness studies for virtually all of the major medical problems. Accordingly, these estimates can be compared meaningfully to estimates for diseases, such as cancer, stroke, heart disease, diabetes, alcohol abuse and mental illness.

The report noted that between 1992 and 1998 the overall cost of drug abuse to society increased at a rate of 5.9 percent annually and that the rate of increase in costs was in excess of the combined increase of 3.5 percent for the adult population and consumer price index for all services for this period.

The following tables reflect the cost categories and estimates for each estimate segment.

The report noted that the societal cost related to the three major categories of costs and that related to crime remained relatively constant between 1992 and 1998. However, it did not include the estimated $98 billion a year (Drug Enforcement Administration, 2008) that Americans spend on illegal drugs and did not account for the drug use impact on learning among elementary, secondary, and college students.

Although critics may shudder, applying a reasonable 5 percent a year increase to costs, it is likely that the 2008 estimates, if developed by the same methodology as used in 2001, would project social costs of illegal drug abuse in the United States to approximately $230 billion a year.

Costs attributed to alcohol abuse parallel those for illegal drug use. The most recent comprehensive assessment of the social costs of illegal drug use occurred in 2000 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) that estimated the economic costs for alcohol abuse to be almost $185 billion a year (Harwood et al., 1998).

Similar to the estimates for illegal drug use, the largest component was for loss productivity (72.7 percent), with health-related costs contributing 14.3 percent and other costs (crashes, fires, criminal justice etc.) contributing 13 percent.

Again, applying a reasonable 5 percent a year increase in costs, it is likely that the 2008 estimates, if developed by the same methodology as used in 2000, would project social costs of illegal drug abuse in the United States to approximately $300 billion a year.

The efforts to produce useful results have included controversy surrounding the issue of what is to be counted and how. The task of estimating the social costs of substance abuse requires a broad

calculus, and the choice of a framework is not only a technical, scientific issue but also a matter of political philosophy. The conclusions reached through this extrapolation suggest that current estimates of the social and economic costs of illegal drug use and alcohol abuse could reach $500 billion a year.

See also **Accidents and Injuries from Alcohol; Accidents and Injuries from Drugs; Driving, Alcohol, and Drugs; Economic Costs of Alcohol and Drug Abuse; Industry and Workplace, Drug Use in; Productivity: Effects of Alcohol on.**

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SOUTH AFRICA. The use of alcohol and other drugs in southern Africa stretches back more than a millennium. It is likely that the agricultural revolution that involved the domestication of grains was closely associated with the fermentation of those plants to produce alcohol. Even before the development of settled agriculture, in areas dominated by hunting and gathering peoples, substances such as wild fruits and honey provided the basis for making alcoholic drinks of various kinds. In addition, within every region, people exploited rich botanical resources that included many plants believed to possess various pharmaceutical properties and, in some cases, psychoactive powers. Cannabis certainly has a long history in the region, although very little is known about the history of cannabis or other local drug substances on the continent. Early reports regarding the native

peoples of the Cape region indicated their taste for various kinds of alcohol as well as cannabis and other local narcotic plants.

THE COLONIAL PERIOD

Soon after the founding of the Cape of Good Hope Colony in the mid-seventeenth century, European officials and employers began to use liquor, tobacco, and cannabis as payment for work, and these kinds of labor arrangements were commonplace by 1800. A local desert root plant, known as *dagga*, was gathered, traded widely, and chewed. It apparently faded in importance during the 1700s, however, and was replaced by *canna*, a plant that was made into a drink reputed to induce a "frenzy most horrible to behold" (Gordon, 1996, p. 69). The use of these mild narcotics persisted well into the nineteenth century, and they spread among neighboring African peoples. Stronger alcoholic drinks, imported from Europe and produced in the expanding colonial economy, steadily pushed the indigenous drugs to the margins, however. Records indicate that local societies easily incorporated alcohol consumption, but that they were unfamiliar with smoking.

Cape Town was initially established as a provisioning station for the Dutch trade with the East Indies, but the port town quickly gained the nickname, "Tavern of the Seas." Some of the early white settlers established vineyards, and winemaking developed into a major industry. Cape wines were generally low quality, but they became an important element in the local and regional economies, which was based, for the most, part on the utilization of slave labor. Vineyard owners were soon converting their wines into cheap brandy known as "Cape Smoke." Labor patterns that rewarded work with brandy rations became a key element in the wine production system.

After the transfer to British rule around 1800 and the abolition of slavery several decades later, the *dop* system, by which brandy allotments were part of workers' wages, helped keep workers in semi-bondage. During the nineteenth century, the provision of these liquor payments, coupled with the cheap and easy availability of Cape Smoke, sustained a culture of excessive alcohol consumption and alcohol abuse among Colored (mixed-race) workers. Well into the twentieth century, the white vineyard owners continued to hold the kind of political clout that thwarted any efforts to reform the system. Thus, when employers in much of the rest of the country pressed for regulation to ensure a sober and disciplined workforce, the vineyard owners and their allies essentially saw sobriety as an enemy of discipline and control. Moreover, they were concerned with maintaining the large market for their products that the black population of the region represented. This system was created within a white-dominated society for which alcohol consumption was a critical element of social and economic life. Whites did not, therefore, regard the cheap brandy that they produced as dangerous, but South African whites did develop persistent stereotypes of the black and Colored population as innately attracted to alcohol.

BEER PRODUCTION IN THE NINETEENTH CENTURY

As Dutch-speaking white settlers and traders pushed into the interior of South Africa during the nineteenth century, they confronted and came into conflict with large populations of settled agriculturalists, such as the Xhosa, Zulu, Sotho, and Tswana. These peoples all had well-established traditions of producing grain-based beers, mostly produced through female labor. These beers were typically very thick, fermented drinks with a very limited shelf life, and their production was closely tied to the agricultural cycle. "Beer drinks" were almost always communal affairs held to mark important events, such as weddings and funerals. Beer was also used as a reward for help in accomplishing tasks that exceeded the capacity of family units to manage. And while they were primarily social affairs, beer drinks could also be highly ritualized reproductions of hierarchy. As such, they were typically dominated by adult men, although women were sometimes provided with drinks as well.

Grain beer was also a form of tribute, and it was commonplace during the harvest season for lines of people to offer calabashes of these beverages to local chiefs and rulers, such as the Zulu and Sotho kings, who played critical roles in nineteenth-century South African history. These leaders were themselves among the relatively small number of men who could command the labor resources to produce very large quantities of beer, and they had stores of grain adequate to produce alcohol throughout the year. This helped them to maintain their courts and attract followers.

The use of beer as tribute payment also accentuated sharp differences in wealth and status. The production of beer in rural agricultural societies represented a diversion of a critical food resource to the production of alcohol. Local grain beers certainly had food value, but beer production nevertheless shifted food supplies away from peripheral family members and dependents. This practice could therefore have dire impact during times when grain stocks ran low or disappeared.

CHRISTIANITY AND EARLY TEMPERANCE MOVEMENTS

By the middle of the nineteenth century, substantial areas of African settlement had been under white control for decades, and growing numbers of Africans had converted to Christianity. Many of these people settled into Christian communities that valued hard work, commerce, education, and devotion. Among these people, temperance gained substantial support, and the temperance organizations that formed represented not only efforts to reduce or eliminate drinking but nascent political movements as well. As Christianity spread, temperance spread with it, and South Africa evolved into a society in which a substantial portion of the population abstained, or claimed to abstain, from drink. Abstinence also found support among the sizeable Colored Muslim population based in Cape Town and surrounding areas.

The spread of commerce into the South African interior also involved the expansion of the liquor trade, notably brandy and other spirits. African leaders, such as Moshoeshoe in Lesotho and, later, Khama in Bechuanaland, attempted to resist the liquor trade, seeing these drinks as dangerous and fundamentally different from the traditional grain beers, which had a low alcoholic content and were regarded as foods. Cannabis smoking was also apparently quite widespread in African farming communities, but the evidence does not really make clear how common it was or in what circumstances smoking took place.

INDUSTRIALIZATION AND ALCOHOL AND DRUG CONTROL

The discovery of diamonds and gold in the interior of South Africa during the last part of the nineteenth century transformed the political economy of the region. Capital poured into the area and modern mining operations were established. These new industrial enterprises attracted migrants from across southern Africa, Europe, and Asia—especially to the new urban complex surrounding Johannesburg. During the early twentieth century, the area known as Witwatersrand became the hub of a huge migrant labor network that brought in young male contract workers from their rural homes, often hundreds of miles away to the north. Industrialization also set off a contest for territory that resulted in the defeat of the last independent African polities and the triumph of British imperial power, which culminated in the formation of the white-dominated Union of South Africa in 1910.

The urbanization and industrialization of South Africa resulted in two distinct approaches to the control of African drinking. Africans who migrated into the cities, whether permanently or temporarily, carried with them their existing drinking practices—although the young men who made up the bulk of the new migrants did not typically drink a great deal in their rural homes. In the cities, however, they found themselves within an industrial regime that often confined them to male-only residential hostels or compounds. In the late nineteenth century, a distillery was established in Johannesburg to supply African drinkers, who typically had little if any experience with distilled drinks. This successful enterprise soon provoked a backlash from white civic leaders and employers, who feared that excessive drinking would lead to crime and undermine worker discipline.

As part of a broader process of establishing progressively closer control over urban Africans, prohibition was imposed on Africans in 1897, and this ban remained in place until the 1930s. This measure probably succeeded in limiting drinking, especially of spirits, but it also led to the emergence of a network of criminal gangs that profited from distributing illicit alcohol. It also led to the development of a *shebeen* subculture in urban neighborhoods. These illegal drinking establishments—which were sometimes quite elaborate, but often little more than backrooms—became important centers of social life and focal points in the development of distinctive urban styles and tastes. Shebeen proprietors were almost always women, and they were the targets of continual police harassment. Indeed, by the 1950s more than 200,000 black South Africans were being convicted annually for liquor offenses. In 1959 the

anger of Durban's women brewers exploded in riots in the working-class neighborhood of Cato Manor, and this was just one of a series of such protests across the region.

In the South African city of Durban, a different model of liquor control developed, one that eventually was adopted across the country and throughout much of eastern and central Africa. The "Durban system" involved restricting African drinking to municipally owned beer halls and using the substantial profits from these enterprises to fund the creation of segregated African residential areas and services. Illicit producers and sellers challenged this system, and the beer halls became for many one more symbol of white domination under apartheid. In the Cape region, the power of the wine growers prevented prohibition or even serious state restriction on the distribution and consumption of alcohol.

South Africa, following trends in Europe, the United States, and British colonial Africa, also imposed prohibitions on drugs such as cocaine and cannabis. In the postwar era, as South Africa evolved into a moralistic police state, drug use was pushed further under cover, but cannabis smoking was certainly an element of the vibrant urban youth culture that developed in black communities in the 1950s. When the drug revolution hit Europe and the United States in the 1960s, cannabis use also spread to white youths in South Africa. The repression and stress associated with life under the racially stratified white regime encouraged alcohol abuse among both Africans and whites, and mood-altering pharmaceuticals also grew in popularity.

From the 1960s on, the regime made efforts to liberalize alcohol regulations to give African consumers access to spirits, and eventually it legalized some shebeens. Nevertheless, until the apartheid system began to break down in the 1980s, the distribution and consumption of alcohol and illegal drugs (and indeed the customs of consumption) continued to be structured along racial lines. When youths in the massive Johannesburg ghetto of Soweto launched their revolt against the authorities in 1976, among the very first targets of their attacks were the state-owned liquor stores.

THE TRANSFORMATION OF THE ALCOHOL INDUSTRY

In South Africa in the early twenty-first century, the consumption of alcohol continues to be an important leisure activity. Adult alcohol consumption per capita was estimated in 2000 to be 12.4 liters per year (incorporating unrecorded consumption), which was considerably less than in many other countries. However, the amount consumed per drinker approached 20 liters, which was among the highest levels in the world at the time. In addition, a 1998 survey found that one-third of adult drinkers engaged in risky weekend binging (Parry, 2005, p. 426). Excessive consumption is facilitated by many customary drinking practices in South Africa, including public drinking, communal drinking, and the provision of large amounts of alcohol at weddings, funerals, and other ceremonies. Overall alcohol consumption appears to be stable, although there are trends away from "traditional" sorghum beer and toward spirit coolers and alcoholic fruit drinks. An increase in the proportion of younger men and women who are drinking has also been reported, suggesting that the percentage of abstainers in the population may be declining (Parry, 2005, p. 426).

In South Africa, as elsewhere, there is a close connection between the consumption of alcohol and illegal drugs and risky sexual behavior. This linkage is particularly ominous in South Africa, given the high levels of HIV infection among the nation's youth. South Africa has also recorded some of the highest rates of fetal alcohol syndrome ever observed. Alcohol abuse and associated social and health problems reflect a history of racial stratification and extreme inequality. Since the end of apartheid and the institution of democratic rule in the mid-1990s, notwithstanding robust economic growth, the state has lacked the resources to provide adequate, or even basic, health services to the substantial proportion of the population living in poverty. Alcohol and drug treatment programs are even more difficult to find. Moreover, as they have historically, alcohol sales continue to provide substantial revenues to official budgets. Since the late 1990s, the government has raised alcohol taxes, however, with the combined goals of increasing revenue, limiting drinking, and encouraging the consumption of drinks with lower alcohol content.

These efforts must contend with an aggressive corporate sector that actively promotes an array of alcoholic drinks through sophisticated promotional strategies. A small number of large companies have

long held control over the production, importation, and distribution of spirits and European-type beer. The end of apartheid, meanwhile, along the concomitant elimination of international restrictions on trade with South Africa, has provided great opportunities for these companies to consolidate their positions and increase their sales, in particular in other African countries where they were largely forbidden to operate during the apartheid era. The South African Breweries Ltd. (SAB) experienced an especially dramatic period of growth, and by 2000 it had captured 98 percent of the South African market for bottled beer. The company was a pioneer in providing job and professional advancement opportunities for employees of color, and as a result it was able to build a strong working relationship with the African National Congress when it came to power in 1994. Building on its African base, the SAB repositioned itself as a global corporation. In 2002 the company acquired the U.S.-based Miller Brewing Company and shifted its headquarters to London, and it has become one of the four largest brewing companies in the world. On a smaller scale, winemaking concerns have systematically improved the quality of their products and aggressively pursued the international market.

Since the 1980s, the reduction and/or elimination of race-based restrictions on the sale of alcohol have combined with privatization to make this an attractive area for small businesses. Not surprisingly, the legalization of shebeens has encouraged small-scale businessmen to move into an area that was largely controlled by women when these establishments were illegal.

SOUTH AFRICA AND THE DRUGS TRADE

The international boycott of Apartheid-era South Africa, the country's ongoing confrontation with its neighbors to the north, and the related close scrutiny by the South African regime of its own borders have all had the effect of limiting the drug trade in South Africa. The transition to majority rule in the early 1990s had the ironic impact of not only removing barriers to legal commerce, but also to trade in illegal substances. By the mid-1990s, however, reports had begun to appear in the international media that South Africa was emerging as an important trans-shipment point for heroin and cocaine. Thus, the recent history of South Africa's drug use and engagement with international drug trafficking, to a substantial extent, fits within the broader pattern of Africa as a whole. However, it also reflects South Africa's distinctive history of racial stratification, in particular in the popularity of the depressant methaqualone (Mandrax), hallucinogenics, and drugs such as Ecstasy that have been much more popular in Europe and North America than in Africa. As major South African cities have been drawn into the international heroin commerce, local use has apparently also increased dramatically (although estimates vary widely). Until recently, at least, heroin use remained confined largely to the whites and to the Colored (or mixed-race) population. In contrast to other parts of the world, smoking remains the most prevalent use of heroin consumption in South Africa.

Since 2000 South Africa has become an important methamphetamine center, particularly as the production and distribution of the synthesized drug has become increasingly globalized. Between 2004 and 2005 the importation into South Africa of pseudoephedrine, a key ingredient in the drug, grew by 1,300 percent. Much of South Africa's methamphetamine production is exported regionally and internationally, but the cost has been so low that a great deal has also spilled over into the local drug market. Although evidence is sparse, it appears that drug trafficking in South Africa is linked to networks of immigrants from other African countries, notably Nigeria. The number of migrants in the country increased sharply after the end of white rule, and whether fairly or unfairly, immigrants are often blamed for criminal activities and drug trading.

The most common drug used in Cape Town, and elsewhere in South Africa, remains cannabis. It is widely grown, but remote rural areas such as Lesotho dominate the trade. Little is known about the organization of the traffic, but the product tends to be carried along existing commercial and migrant labor routes into South Africa's cities. There have been substantial confiscations of sacks of cannabis in raids on migrant labor hostels.

The dismantling of the elaborate and repressive system of population controls associated with apartheid created a much more liberal social and cultural environment. However, the optimism associated with majority rule was soon dampened by the realities of unemployment, persistent poverty, and

urban decay, which have created breeding grounds for alcohol and drug abuse. Popular concerns, particularly among the urban masses, were increasingly focused on economic and security issues. Beginning in the mid-1990s, these trends spawned a number of populist antidrug and anticrime crusades. In perhaps the most notorious example, in 1996 a Cape Town Muslim organization, People Against Gangsterism and Drugs (PAGAD), confronted a suspected drug dealer named Rashaad Staggie, who headed the Hard Livings gang. A motorcade of some 500 vehicles converged on his headquarters, and PAGAD members captured Staggie, set him on fire, and eventually shot him dead. No one was convicted of the murder, although organization leaders were ultimately found guilty of public violence. In the aftermath of these events, claims were made that the attack had been staged by rival drug dealers, illustrating both the growing pervasiveness of drug-trading gangs and the growing public alarm about drug use and the drug trade.

By the mid-1990s, the growing alarm about the rising consumption of illegal drugs had caused the new South African regime to enlist in the U.S.-sponsored "global war on drugs" and seek American government assistance in combating local drug use and drug trading. Nonetheless, drugs such as cocaine, crack cocaine, and cannabis continue to be easily available in the urban areas of South Africa.

In 1999 the Youth League of the ruling African National Congress prepared a policy on substance abuse that denounced the abuse of alcohol and drugs as deeply destructive of community and family life, reflecting the ANC's established moralistic tradition. Not surprisingly, most attention focused on alcohol. But given the close relationship between corporate and state interests in South Africa, the policy did not advocate abstinence and prohibition strategies, but rather the promotion of responsible drinking.

See also **Africa; Foreign Policy and Drugs, United States; International Drug Supply Systems; Kenya; Nigeria.**

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SPAIN. Spain is a Mediterranean European Union (EU) country with about 46,063,000 inhabitants as of 2008. Its administration is divided into 17 regions (Autonomous Communities), each with a high degree of legislative and executive autonomy. This entry presents information relating to Spain as a whole; however, differences among regions exist because of the country's decentralized political structure.

HISTORY OF SUBSTANCE USE IN SPAIN

Before the mid-1960s, alcohol and tobacco were practically the only drugs consumed in Spain. Both were (and remained into the early twenty-first century) legal and widely accepted, but risks associated with their consumption were underestimated. Until the mid-1970s, the use of illicit drugs was rare. Spanish people did not begin to see drugs as a problem until the end of the 1970s. In fact, in 1979, the

Ministry of Health created the first drug abuse treatment centers. However, between the end of the 1970s and the mid-1980s, the consumption of drugs, and in particular heroin injected intravenously, increased sharply, along with an increased frequency of HIV/AIDS cases among these drug users. The use of drugs also became associated with delinquency and marginalization, causing alarm.

The alarm was so great, in fact, that the government created the 1985 National Plan on Drugs to coordinate and enforce regional governmental policies and various social entities. Regional Plans on Drugs were also created, and centers to treat drug dependent patients were established. These services were available to everyone since Spain has universal health care.

From the mid-1980s until the early twenty-first century, the situation changed radically, especially regarding illicit drug use, which became widespread. In fact, as of 2008, Spain had one of the highest levels of consumption of cannabis and cocaine in the world, although heroin use and its associated diseases have decreased. In contrast with the 1980s, consumption of cannabis, synthetic drugs, and cocaine is more often connected to the culture of leisure rather than with delinquency.

TRENDS AND PATTERNS OF SUBSTANCE USE

The main sources of information in Spain on the patterns of drug use are those obtained through the *Home Survey on Drug Abuse in Spain* (EDADES) (DGPND, 2006) and the *State Survey on Drug Use in Secondary Education Students* (ESTUDES) (DGPND, 2007). The questionnaires and methodology used in these surveys are similar to those used in other EU countries.

Home Survey on Drug Abuse in Spain (EDADES): This survey has been carried out every other year since 1995 among the population from 14 to 65 years of age, except for 1995, in which no upper age limit was established. As of 2008, the data from 1995 to 2003 were available, whereas only the preliminary data of the studies from 2005 to 2007 were available (see Table 1).

State Survey on Drug Use in Secondary Education Students (ESTUDES): This survey has been carried out every other year since 1994. It gathers information concerning illicit drug use among students between 14 and 18 years of age.

Alcohol was the most frequently consumed drug in Spain, though between 1975 and 2005 there was an important change in the consumption pattern. The daily consumption of alcohol decreased, and the consumption of wine (typical in the Mediterranean diet) decreased. By contrast, the consumption of beer increased and the consumption of alcohol used only on weekends increased. Among students (aged 14 to 18) *binge drinking* (defined by the Ministry of Health as the intake of at least 60 g of alcohol in men or 40 g in women in a single drinking session and in which the person becomes intoxicated with a blood alcohol concentration of 0.8 percent or higher) increased. One statistic showed that the frequency of drunkenness in a test group in the 30 days prior to the survey rose from 20.7 percent in 1994 to 34.8 percent in 2004. Alcohol consumption was responsible for 2.08 percent of all deaths. Alcohol consumption per capita decreased in the early twenty-first century as Spanish people began to see the associated health problems.

The consumption of tobacco is responsible for 6 percent of all deaths according to several studies (González Enríquez et al., 1997; Banegas et al., 2005). Since the year 2000, a decrease in the daily consumption of tobacco has been noted, although this decrease can be seen mostly in men, where the decrease among women is much less. In fact, among young people, smoking is more common among women than among men. In the 1970s and 1980s most people smoked French-type tobacco known as *black* tobacco, whereas in the early twenty-first century the great majority smoked American-type *blond* tobacco. But people are increasingly aware of the health consequences of tobacco use. In the early twenty-first century, antismoking advice was provided at the primary-care service level, by physicians and other health-care professionals who have direct contact with patients, and several units specializing in tobacco addiction were created. Whereas the Public Health Service pays for the pharmacological treatment of various illnesses, as of 2008 pharmacological treatment to combat tobacco addiction was not reimbursed (it was paid for by the patient in contrast to medication for other diseases, which was free).

	1995	1997	1999	2001	2003	2005
Prevalence of consuming at some time during life						
Tobacco	—	69.7	64.9	68.4	68.9	69.5
Alcohol	—	90.6	87.3	89.0	88.6	93.7
Cannabis	14.5	22.9	19.6	23.8	29.0	28.6
Ecstasy	2.0	2.5	2.4	4.0	4.6	4.4
Hallucinogenics	2.1	2.9	1.9	2.8	3.0	3.4
Amphetamines/Speed	2.3	2.7	2.2	2.9	3.2	3.4
Cocaine powder	3.4	3.4	3.1	4.8	5.9	7.0
Cocaine base	0.3	0.4	0.4	0.5	0.5	0.6
Heroin	0.8	0.6	0.5	0.6	0.9	0.7
Other opiates	0.2	0.5	0.3	0.6	0.4	0.5
Inhalable volatiles	0.7	0.8	0.6	0.8	1.0	0.8
Prevalence of consuming in the previous 12 months						
Tobacco	—	46.8	44.7	46.0	47.8	42.4
Alcohol	68.5	78.5	75.2	78.1	76.6	76.7
Hypno-sedatives without medical prescription	12.3	2.3	2.3	2.8	3.1	—
Cannabis	7.5	7.7	7.0	9.2	11.3	11.2
Ecstasy	1.3	0.9	0.8	1.8	1.4	1.2
Hallucinogenics	0.8	0.9	0.6	0.7	0.6	0.7
Amphetamines/Speed	1.0	0.9	0.7	1.1	0.8	1.0
Cocaine powder	1.8	1.6	1.6	2.5	2.7	3.0
Cocaine base	0.1	0.1	0.2	0.1	0.1	0.2
Heroin	0.5	0.2	0.1	0.1	0.1	0.1
Other opiates	0.1	0.1	0.1	0.2	0.1	0.1
Inhalable volatiles	0.1	0.2	0.1	0.1	0.1	0.1
Prevalence of consuming in the last 30 days						
Tobacco	—	42.9	40.1	41.4	42.9	38.4
Alcohol	—	64.0	61.8	63.7	64.1	64.6
Cannabis	—	4.6	4.5	6.4	7.6	8.7
Ecstasy	—	0.3	0.2	0.8	0.4	0.6
Hallucinogenics	—	0.2	0.2	0.2	0.2	0.2
Amphetamines/Speed	—	0.2	0.3	0.6	0.2	0.4
Cocaine powder	—	0.9	0.9	1.3	1.1	1.6
Cocaine base	—	0.0	0.1	0.0	0.0	0.1
Heroin	—	0.1	0.0	0.0	0.0	0.1
Other opiates	—	0.1	0.1	0.1	0.1	0.1
Inhalable volatiles	—	0.1	0.0	0.1	0.0	0.1
Prevalence of daily consumption in the last 30 days						
Tobacco	—	34.9	33.6	35.7	36.7	32.8
Alcohol	—	12.7	13.7	15.7	14.1	14.9
Cannabis	—	0.7	0.8	1.5	1.5	2.0

Table 1. Evolution of the prevalences in the consumption of psychoactive substances among the population aged 15–64. Results of the Home Surveys on Drug Abuse (EDADES). Spain 1995–2003 (DGPND, 2006). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

Heroin use was particularly high at the end of the 1970s and during the 1980s. For many years, Spain had one of the highest rates of AIDS in the world: In 2002, according to the Euro HIV Web site, the number of HIV/AIDS cases among intravenous drugs users was 30 per million inhabitants. The number of new cases of AIDS diagnosed among intravenous drug users increased in 1994 (5,082) and declined after that (1995: 4,733; 1997: 3,153; 1999: 1,811, 2001: 1,305; 2003: 1,102; 2005: 811; DGPND, 2008). Heroin consumption continued thereafter to decrease, and as of 2008 it was ever more difficult to find young heroin addicts. As of 2008, the great majority of heroin users consume other substances, especially cocaine. Injected heroin and needle sharing has become rare. Harm reduction approaches, including use of prescribed methadone, has contributed to controlling the medico-social problems of these patients, in particular AIDS and Hepatitis C. The consumption of other opiates is rare. Buprenorphine and naloxone were introduced in therapeutic treatment, but the cost is not covered by the Public Health Service.

In the early twentieth century, cannabis was the most popular illicit drug in Spain and was being

	1994	1996	1998	2000	2002	2004	2006
Prevalence of consuming at some time during life							
Tobacco	60.6	64.4	63.4	61.8	59.8	60.4	46.1
Alcohol	84.1	84.2	86.0	78.0	76.6	82.0	79.6
Hypno-sedatives	6.1	6.1	6.4	6.9	6.5	7.0	7.6
Cannabis	20.9	26.4	29.5	33.2	37.5	42.7	36.2
Ecstasy	3.6	5.5	3.6	6.2	6.4	5.0	3.3
Hallucinogenics	5.1	6.8	5.5	5.8	4.4	4.7	4.1
Amphetamines/Speed	4.2	5.3	4.3	4.5	5.5	4.8	3.4
Cocaine	2.5	3.4	5.4	6.5	7.7	9.0	5.7
Heroin	0.5	0.5	0.9	0.6	0.5	0.7	1.0
Inhalable volatiles	3.1	3.3	4.2	4.3	3.7	4.1	3.0
Prevalence of consuming in the previous 12 months							
Alcohol	82.7	82.4	83.8	77.3	75.6	81.0	74.9
Hypno-sedatives	4.4	4.5	4.7	5.0	4.5	4.7	4.8
Cannabis	18.2	23.4	25.7	28.8	32.8	36.6	29.8
Ecstasy	3.2	4.1	2.5	5.2	4.3	2.6	2.4
Hallucinogenics	4.4	5.6	4.0	4.2	3.2	3.1	2.8
Amphetamines/Speed	3.5	4.4	3.4	3.5	4.1	3.3	2.6
Cocaine powder	1.8	2.7	4.5	4.8	6.2	7.2	4.1
Heroin	0.3	0.4	0.6	0.4	0.3	0.4	0.8
Inhalable volatiles	1.9	2.0	2.6	2.5	2.2	2.2	1.8
Prevalence of consuming in the last 30 days							
Tobacco	31.1	32.5	31.9	32.1	29.4	37.4	27.9
Alcohol	75.1	66.7	68.1	60.2	56.0	65.6	58.0
Hypno-sedatives	2.6	2.2	2.3	2.5	2.4	2.4	2.4
Cannabis	12.4	15.7	17.2	20.8	22.5	25.1	20.1
Ecstasy	2.1	2.3	1.6	2.8	1.9	1.5	1.4
Hallucinogenics	2.6	2.8	2.0	2.0	1.2	1.5	1.3
Amphetamines/Speed	2.3	2.6	2.0	2.0	2.0	1.8	1.4
Cocaine	1.1	1.6	2.5	2.5	3.2	3.8	2.3
Heroin	0.2	0.3	0.4	0.3	0.2	0.4	0.5
Inhalable volatiles	1.1	1.2	1.8	1.5	1.1	1.1	1.1

Table 2. Evolution of the prevalence of the consumption of psychoactive substances among secondary education students 14–18 years of age. Results of the State Surveys on Drug Use in Secondary Education (ESTUDES). Spain 1994–2006 (DGPND, 2007). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

consumed at ever earlier ages. Although usually sporadic, consumption has increased considerably (Tables 1 and 2). There is a low perception of risks associated with cannabis and an increase in related hospital-treated emergencies.

Cocaine is the second most consumed drug in Spain, and its consumption has been rising. However, a student survey of 2006 (Table 2) showed a decrease in the prevalence of cocaine consumption, which must be confirmed in later studies. The information available showed an increase in requests for treatment, mortality, and hospital-treated emergencies related to cocaine use.

The use of amphetamines and other synthetic drugs began to increase in the mid-1990s. For a long time they enjoyed great popularity and a low perception of health risks. It is frequently difficult to ascertain exactly which group of substances is being consumed, as people sometimes consume amphetamines believing that it is Ecstasy. Ecstasy, the street name for methylenedioxymethamphetamine or MDMA, is a semisynthetic drug in a subclass within the larger class of amphetamines. The consumption of LSD and other hallucinogenic drugs is infrequent.

REGULATIONS FOR LEGAL AND ILLEGAL SUBSTANCES

Because of Spain's decentralized political structure and the high degree of autonomy of its 17 regions, legislation concerning alcohol, tobacco, and illegal drugs can be either national, covering the whole of Spanish territory, or regional. In some cases, the national government makes the general rules, while the regional government has to make specific legislation within the general framework; thus differences among regions exist.

Regulations on alcohol are similar to those of other EU countries. For instance, it is illegal to

drive with a blood alcohol concentration over 0.5 grams of alcohol per liter of blood (or 0.25mg of alcohol per liter of air in the lungs), 0.3 grams per liter of blood (0.15mg of alcohol per liter of air in the lungs) for professional or newly licensed drivers. The sale of alcohol to those under 18 years of age is prohibited, and restrictions apply to advertising. Given the growth in binge drinking among young people, there have been two attempts to pass a national law to regulate the consumption of alcohol by those under age 18. In both cases, the proposal was scrapped due to strong public and industry opposition.

An anti-tobacco law (Ley 28/2005) went into effect on January 1, 2006, prohibiting smoking in public places (e.g., the workplace, cultural centers). The law differentiates between areas in which smoking is totally forbidden and areas in which it is permitted (e.g., restaurants) if a special area for smokers is created.

The private consumption of drugs is not a chargeable offense in Spain. However, "consumption in public places, streets, establishments or public transport, as well as the illicit possession, even though it is not for trafficking, and the abandonment in the aforementioned places of instruments used for consumption" is considered an offense that carries a fine. Spain's penal code distinguishes between drugs that cause serious harm to a person's health and those that do not. All street drugs are considered harmful except for cannabis and benzodiazepines. The law punishes drug production (cultivation, elaboration, manufacture), as well as acts of drug trafficking (sale or exchange), prior acts (such as possession or the transport of drugs for the purposes of trafficking), and acts to encourage consumption (promoting, favoring, facilitating). In addition, driving a motor vehicle under the influence of any kind of drug is a chargeable offense. Efforts to control the supply of drugs and various other criminal activities such as drug trafficking, money laundering, and other related crimes were being developed in the early twenty-first century.

POLICIES ON ALCOHOL, SMOKING, AND ILLEGAL DRUGS

The Ministry of Heath and the regional health administrations are responsible for policy development. Illegal drugs policies are the responsibility of the National Plan on Drugs and Regional Plans on Drugs, whereas policies regarding alcohol and tobacco belong to either of these bodies or the Public Health Servicies.

In 2000, the National Drugs Strategy 2000–2008 (DGPND, 2000) defined its course of action and goals. Its strategy was based on the following:

- Coordination of all those working in the drug field
- Social prevention and awareness building through education and personal development
- Integration of drug user care
- Improvement in knowledge of drugs
- Reduction in the supply through increased police and customs effectiveness in handling drug trafficking
- International cooperation

Trends in alcohol, smoking, and illicit drug use in Spain in the last decades of the twentieth century show marked changes. Alcohol consumption patterns have changed noticeably, with beer drinking on the weekends increased. Alcohol consumption per capita decreased, and awareness regarding the consequences of alcohol consumption improved. Underage drinking remained a concern. Alcohol use has health, legal, and social consequences, but the government failed twice to introduce new regulations due to public resistance and industry lobbies. Smoking has started to decline, particularly among males, and the general population is concerned about the health consequences of smoking. Regarding illicit drugs, Spain has some of the highest rates of use in the world. Cannabis is the favorite drug, followed by cocaine, and synthetic amphetamines. Drug use moved from marginalization and delinquency (heroin use epidemic in late 1980s) to the culture of leisure (cannabis, cocaine, synthetic drugs). Cannabis, and to some extent synthetic drugs, are seen as harmless. However, illicit drugs use still generates a lot of health, legal, and social consequences, while the efforts carried out by the national and regional policies to some extent failed to decrease drug use and its consequences. Drug treatment has become increasingly integrated in the public health system. At the same time, smoking and alcohol treatment counseling (e.g., brief intervention) are more and more frequently offered at primary care services.

See also **European Union; Foreign Policy and Drugs, United States; France; International Drug Supply Systems; Italy.**

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F. JAVIER ALVAREZ

SPORT, DRUGS IN INTERNATIONAL. There are extensive social, cultural, historical, and economic connections between drugs and sport. Although a great deal of international attention is given to performance enhancing drugs, the weight of harm associated with drug use as it relates to sport, lies with alcohol. In addition to exploring the issues related to performance enhancing drugs, this section focuses on the relationships between alcohol and sport.

DEVELOPMENT OF DRUG USE IN SPORT

Ancient Greek athletes were known to use special diets and potions in the ancient games, and in modern sports (professional and amateur) the use of artificial stimulants (performance enhancing drugs) may have been in widespread use since the nineteenth century (Yaselis et al., 2001). The emergence of modern pharmaceuticals in the early twentieth century was perhaps influential in the development of drug use in sport (Wilson & Derse, 2001). The World Anti-Doping Agency (WADA) asserts that in 1928 the International Amateur Athletic Federation (IAAF) became the first international athletics organization to ban the use of stimulating substances.

Stokvis (2003) suggests that in 1933 a member of the French National Olympic Committee lodged the first official complaint about the use of stimulant substances among amateur athletes. The nature of the complaint was that the use of injections among athletes at the 1932 Olympic Games was a sign of dishonesty. Stokvis also asserts that in 1938 the International Olympics Committee (IOC) decided to disallow drug-using athletes to compete in the games; however, it was not until the 1960s that doping became a subject of formal regulation. In 1963 the Council of Europe agreed on a draft convention against the use of performance enhancing drugs in sport, which was later ratified in 1989 (Council of Europe, 1989).

Increased appreciation of the extent and complexity of doping following a drug-doping incident in cycling in 1998 resulted in the Lausanne Declaration on Doping in Sport. The World Anti-Doping Agency, established in 1999, formed out of the Lausanne Declaration, with a mandate to promote and coordinate strategies to prevent doping in sport internationally. The formation of WADA effected a series of consultations to develop an international anti-doping code. Starting from the International Drugs in Sport Summit in Sydney 1999, the International Intergovernmental Consultative Group on Anti-Doping (IICGAD) in Sport met annually until

Adverse test results (detected drug)	Number of adverse results	Percent of total adverse test results
Anabolic agents	1,966	45.4%
Beta-2 agonists	631	14.6%
Cannabinoids	553	12.8%
Stimulants	490	11.3%
Diuretics and other masking agents	290	6.7%
Glucocorticosteroids	282	6.5%
Hormones and related substances	42	1.0%
Beta-blockers	28	0.6%
Agents with anti-estrogenic activity	30	0.7%
Narcotics	16	0.4%
Chemical and physical manipulation	4	0.1%

SOURCE: World Anti-Doping Agency, http://www.wada-ama.org/rtecontent/document/LABSTATS_2006.pdf (downloaded 10-06-2008).

Table 1. Adverse drug testing results reported by the World Anti-Doping Agency for 2006. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

2003 to develop a series of governance and funding arrangements to support WADA.

For example, it was agreed in 2001 that the five Olympic Regions of the world would contribute differentially to the WADA budget: Africa (0.50%), Americas (29%), Asia (20.46%), Europe (47.5%), and Oceania (2.54%). The regional share percentages were reconfirmed in the 2003 Copenhagen Declaration on Anti-Doping in Sport. The code was the first international agreement harmonizing anti-doping rules across all sports and all nations.

The WADA Foundation Board is now jointly composed of representatives of the Olympic Movement (the IOC, National Olympic Committees, International Sports Federations, and athletes) and representatives of governments from five continents.

DRUGS IN USE, HOW, AND THE EFFECTS

According to statistics from WADA the following drugs (Table 1) are most widely detected in international sport.

Anabolic Agents. Anabolic agents are clearly the most popular drugs used in conjunction with sport internationally (Table 1). Anabolic steroids accelerate the growth of muscle and bone and can subsequently improve the body's capacity for training and competition by reducing fatigue and recovery time. Both naturally produced and synthetically manufactured sources can create anabolic androgenic steroids. Beta-2 agonists are also considered anabolic substances because they can also stimulate tissue growth.

Cannabinoids. Cannabinoids are substances derived from the cannabis plant and are commonly referred to as marijuana. Widely used in the general community, this illicit substance has a variety of depressant effects. Cannabinoids are not considered performance enhancing drugs, but they are prohibited by the WADA code in competition because they pose a risk to the health of athletes.

Stimulants. Stimulants such as amphetamine, cocaine, and ephedrine act directly on the central nervous system to increase alertness, reduce fatigue, and increase competitiveness and aggression. There are mental health, cardiovascular, and dependence risks associated with abuse of stimulants. Stimulants are prohibited in competition under the World Anti-Doping Code 2007 Prohibited List.

The World Anti-Doping Code accepts a range of mild stimulants used for therapeutic purposes; however, it is possible that they are banned in regional or local codes. These stimulants include bupropion, pseudoephedrine, caffeine, phenylephrine, penylpropanolamine, pipradrol, and synephrine.

Diuretics and Other Masking Agents. Diuretics and other masking agents are used to either cause rapid weight loss or to mask the presence of anabolic drugs in urine The health risks associated with diuretics include dehydration, dizziness, headaches, nausea, loss of coordination and balance, cramps, and kidney and heart failure. Diuretics are on the prohibited list, both in and out of competition in all sports as masking agents.

Glucocorticosteroids. Glucocorticosteroids are anti-inflammatory agents used and administered in a variety of ways to treat chronic inflammatory conditions such as arthritis, asthma, inflamed joints, and allergic reactions. Systemically administered glucocorticosteroids are prohibited in competition, whereas glucocorticosteroid use is permitted when applied topically (e.g., with a cream).

Hormones and Related Substances. Hormones and related substances are prohibited in and out of competition under the World Anti-Doping Code. Some hormones are used to stimulate tissue growth,

enhance muscle strength, improve oxygen carrying capacity, and reduce recovery time. The following hormones and related substances are prohibited: corticotrophin (ACTH), erythropoietin (EPO), gonadotrophins, human growth hormone (hGH), insulin and insulin-like growth factor (IGF-1), and mechano growth factors (MGF).

Beta-Blockers. Beta-blockers are drugs that reduce the work of the heart through slowing heart rate and reducing blood pressure. They have been used by athletes competing in sports that require fine motor control such as archery, shooting, curling, and nine-pin bowling or in sports involving control of a vehicle as they can reduce shaking and produce a mild reduction in anxiety without sedation. Beta-blockers are prohibited in competition.

Agents with Anti-Estrogenic Activity. Anti-estrogenic substances serve as masking agents because they may reduce the negative physical side effects of using prohibited anabolic steroids. These include aromatase inhibitors, selective estrogen receptor modulators, and other anti-estrogenic substances.

Narcotics. Narcotic painkillers reduce pain and produce euphoric sensations. This class of drugs includes diamorphine (heroin), morphine, methadone, and pethidine. Because narcotics reduce pain, they can also mask physical damage by reducing the signs of damage. In this respect they are seen as a risk to the health of athletes. Prolonged use may also produce dependence. The use of narcotics is prohibited in competition.

Chemical and Physical Manipulation. The code prohibits tampering or physically manipulating the body or sample collection methods to alter the integrity and validity of biofluid collection. Manipulation can include catheterization or urine substitution.

Alcohol. Alcohol is prohibited in competition only, in selected sports: aeronautic, archery, automobile billiards, boules, karate, modern pentathlon, shooting, motorcycling, and powerboating. A doping violation threshold is established for each sport.

Historically, alcohol has been associated with both sporting participation and with sport spectatorship. Sport has become a significant marketing interest for the alcohol industry. Culturally associated with sociability and sporting celebration, alcohol has occupied an ambivalent place alongside sport, yet there are some troubling dimensions to the alcohol-sport connection that should be explored.

Participation Intensity and Alcohol Consumption. There is a debate in academic literature about the degree to which participating in sport can protect individuals from harmful alcohol consumption or if the participation can actually cause harmful alcohol consumption. It has been generally accepted in the community that participation in sport reduces the likelihood of excessive alcohol consumption. There is, however, a complex relationship between participation in sport and alcohol consumption. In the academic literature there is believed to be a U-shaped curve that relates alcohol consumption to the intensity of sport participation. Both low levels and high levels of sport participation are associated with higher levels of alcohol consumption among adolescents. The association between low levels of sport participation and alcohol use is well documented. Less discussed is the association between high intensity sport participation and high levels of alcohol consumption (Peretti-Watel et al., 2002). Although the U-curve is not uniform for all sports and varies across gender and drug type, the relationship still holds for alcohol consumption among adolescent men (Peretti-Watel et al., 2002).

The social bonding associated with team sports is thought to be an important factor in increasing alcohol consumption among participants above individual performance sports (Garry & Morrissey, 2000; Peretti-Watel et al., 2002).

Although the research is preliminary, alcohol sponsorship may well have a role to play in creating unsafe drinking environments. In a study of the impact of alcohol sponsorship on alcohol consumption among New Zealand amateur sportspeople, Kerry O'Brien and colleagues (2005; 2007) suggest that sponsorship and drink subsidies enhances hazardous drinking among sportspeople.

It is well documented that North American college athletes are a high-risk group for alcohol abuse. The level of alcohol abuse is associated with the level of competition. It has been reported that up to 34 percent of college athletes reported

Performing a density test from urine samples at the Australian Sports Drug Testing Laboratory. AP IMAGES.

consuming at short-term hazardous consumption levels (i.e., bingeing on 11 or more drinks in the past month). Division I athletes are more likely to binge than division III American college athletes (Nelson & Wechsler, 2001). It seems also that alcohol consumption among this group is related to the seasonality of competitive sport as college athletes drink demonstrably less in non-competition times (Martin, 1998).

Sport, Team Bonding, and Alcohol. The playing season can structure an athlete's life by controlling the nature and types of relationships formed, peer networks, and access to alcohol. Data suggest that alcohol consumption varies according to the time of season in competitive sports (Martin, 1998). Heavier drinking in non-competition periods is caused by a number of factors, some of which are individually oriented, whereas others are related to the social nature of sport (Ford, 2007).

The social life associated with adolescent sport can be an important factor in non-competitive sporting environments. In a report on the effects of extracurricular activities on schoolchildren's alcohol consumption, Darling, Caldwell, and Smith (2005) suggest that participation in sporting extracurricular activities increases the likelihood of alcohol consumption above that of non-sporting extracurricular activities. It was suggested that sporting activities provide opportunities for adolescents to mix with adults and to learn from adult drinking behavior. When sporting events involve adult drinking, adolescents can more effectively model adult behaviors.

According to a large-scale North American college survey of hazing (humiliation associated with initiation into clubs, teams or other social grouping) (Allan & Madden, 2008), alcohol plays a major role in hazing behaviors. The most prevalent form of hazing behavior across nearly all student organizations and teams is *participation in drinking games.* Up to 54 percent of varsity sports students reported drinking games as part of hazing behavior. This overshadowed student fraternity clubs where only 20 percent of students reported drinking games as a hazing behavior. The hazardous consumption of alcohol occupies a socially institutionalized role within college sport to a greater extent in North American colleges than other social institutions.

In a study of alcohol consumption among team college sports, Jason Ford (2007) reports that male hockey players in the United States are twice as likely to binge drink, and women soccer players 48 percent more likely to binge drink than other female athletes. It was suggested that rather than the differences emerging from the characteristics of individual athletes, the differential application of social norms in different teams can profoundly shape why participants in teams tend to drink more alcohol than participants in individual sport.

Among specific football codes, results vary. Using a pre-season survey of non-professional rugby players in New Zealand, K. L. Quarrie and colleagues (1996) reported that 78 percent of male players were drinking at hazardous levels. R. J. Maughan (1997) reported an average intake of about 10–12 grams of alcohol per day in the first team squads of two Scottish Premier League teams.

Sport and the Alcohol Industry. The alcohol beverage industry provides a variety of sporting promotions, advertising, and sponsorships through football, motor sports, soccer, and basketball. Global sporting events in particular provide unique opportunities for alcohol producers to connect to large global audiences (Colin & Mackenzie, 2006). There are continuing policy calls to restrict alcohol advertising and sponsorships associated with sport (Klein & Jones-Webb, 2007).

According to WHO (2004a) few countries restrict alcohol industry sponsorship of sporting events, with only about 24 percent of countries having any statutory controls. A majority of countries (68%) do not have restrictions on alcohol sponsorship of sport. Twelve countries have complete bans on sponsorships. Sports sponsorship is banned in Jordan; in Croatia and Turkey sponsorship by the wine and spirits industries is banned, in Bosnia, Herzegovina, Finland, Gambia, Poland and Switzerland the spirits industry is banned.

Drinking at sporting events is the third least restricted drinking environment, with only 26 percent of countries having bans on drinking in sport contexts (WHO, 2004b).

Sports are the perfect vehicle for alcohol marketers to target a young male audience (Howard & Crompton, 1995). Entertainers and athletes are significant role models in shaping purchasing behavior (Martin & Bush, 2000). Athletes are reported to be stronger role models than entertainers in influencing purchasing intentions, especially for young adult male African Americans. It is, however, unclear the precise impact of athletic role models (who promote alcohol beverages) on alcohol consumption among young adults. There is some data suggesting that television beer advertisements in North America are aired most frequently during professional football and basketball games (Madden & Grube, 1994; Snyder et al., 2000; Ellickson et al., 2005).

In 2003 the alcohol industry in the United States spent more than $540 million to place approximately 90,000 ads in sports programs on television. It is estimated that 60 percent of all alcohol advertising on television occurs during sporting events (Center on Alcohol Marketing and Youth, 2003).

In summary, there are significant cultural and market pressures to maintain a strong association between sport and the consumption of alcohol. Although the outcomes from these associations are hotly debated, there is evidence that the saturation of sport can have deleterious effects on athlete performance. It is unclear whether the strong association between alcohol and sport can explain broader trends in hazardous alcohol consumption. It is also unclear whether reducing alcohol advertising on television will have demonstrable effects on binge drinking, as econometric analysis estimates that a 27 percent reduction in television alcohol advertising may result in a 1 percent drop in binge drinking (Saffer & Dave, 2006).

MODES OF CONTROL AND INTERNATIONAL REGULATION

The World Anti-Doping Program is the central mechanism for the international regulation of anti-doping. The program consists of three elements:

Level 1: The World Anti-Doping Code
Level 2: International Standards
Level 3: Models of Best Practice

Underpinning the program is the International Convention against Doping in Sport (2005) and the Copenhagen Declaration on Anti-Doping in Sport (2003).

The 33rd UNESCO General Conference unanimously adopted the International Convention against Doping in Sport in 2005. The convention outlines the conditions through which signatories should prevent, with the view to eliminate doping in sport. The convention under the auspices of UNESCO enables governments to align their domestic legislation with the Code and thereby harmonize sport and public legislation.

The Copenhagen Declaration on Anti-Doping in Sport (2003) is the mechanism through which governments signal their intention to formally recognize and implement the World Anti-Doping Code. At the end of 2007, 192 governments had signed the declaration.

The World Anti-Doping Agency (WADA) administers the World Anti-Doping Program and implements the World Anti-Doping Code. There are seven areas of activity in WADA: code acceptance

	2003	2004	2005	2006
Number of tests	151,210	169,187	183,337	198,143
Adverse results	2,447	2,909	3,909	3,887
Adverse results as a percentage of number of tests	1.6%	1.7%	2.1%	2.0%

SOURCE: World Anti-Doping Agency, http://www.wada-ama.org/rtecontent/document/LABSTATS_2006.pdf (downloaded 10-06-2008)

Table 2. Testing trends in the World Anti-Doping Program (WADP). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

and compliance, science and medicine, out of competition testing, athlete outreach, coordination through the anti-doping management system, anti-doping development, and education. Individual national sporting associations are not bound by the code; however, sovereign countries can introduce regulations that bind national associations to the WADA code.

LIKELY FUTURE DEVELOPMENTS

The level of testing for performance enhancing drugs among professional elite sportspeople through the World Anti-Drug Program has reached a plateau (Table 2). Data from the International Association of Athletics Federations testing program also suggests that testing is widespread and the production of positive tests remains low. Adverse testing rates have also reached a plateau at around 2 percent of total tests.

Unless there are some major advances in the illicit use of performance enhancing drugs, it would seem unlikely that there will be increased rates of adverse test results in the future.

It is likely, however, that national sporting codes will increasingly advocate the beginning of testing regimes for local sports, as they become integrated into the WADA code through national regulatory mechanisms. This will increase the rate of testing in non-elite sporting contexts and no doubt will increase the rate of adverse testing results among players. It is unclear what social and sporting impacts this will have. The desired effect of course will be to reduce drug use among sporting populations. It is, however, unclear whether the testing regimes in non-elite athletes will produce the same preventative effects as it does in elite athletes.

See also **Accidents and Injuries from Alcohol; Accidents and Injuries from Drugs; Advertising and the Alcohol Industry; Cannabinoids; Fashion Industry, International; Foreign Policy and Drugs, United States; International Control Policies; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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SSADDA. *See* **Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA).**

SSAGA. *See* **Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA).**

STILL. Still is the colloquial term for distillery, a device used for distillation—to extract ethyl alcohol (ethanol) from various plants and food products. The simplest ones contain a cooking pot and a tightly fitted cap from which a long arm extends in a downward direction. A mash is boiled, the ethyl alcohol rises to the top and is deposited as a vapor which then condenses as it cools and passes through the arm.

See also **Alcohol: History of Drinking (International); Alcohol: History of Drinking in the United States.**

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STREET VALUE. When drugs are seized by a police or interdiction agency, the significance of the seizure is often measured in terms of its street value; that is, the revenues that would be fetched if each gram were sold at the current retail price.

Such measures are routine among police and customs service agents in the United States and in most other nations, although large price fluctuations can occur from one area to another and within short time frames.

The use of the term *street value* is potentially misleading when it is intended to convey the significance of the seizure as a loss to the traffickers. The price of drugs rises steeply as they move down the distribution chain from point of importation. In mid-2000s, for example, a gram of cocaine could sell on the streets of a U.S. city for about $77. That gram (1,000 milligrams) contained approximately 700 milligrams (mg) of pure cocaine—so that the "pure gram" price was about $109. Yet when sold in 100-kilogram (kg) units at the point of import, the cocaine could have sold for a pure-gram price of about $20. Thus it would cost drug traders $2 million to replace the 100 kilograms. That figure is the total value of payments that would have to be made to growers, refiners, and smugglers in order to obtain another 100 kilograms and bring the drug to the same point in the distribution system.

Valuing a 100-kg seizure at street value would then imply that the government had inflicted a $10.6 million blow to the drug industry, more than five times as much as the true value of the loss. The extent of overstatement increases with the size of the seizure, since the price of drugs goes down as the volume increases in a given transaction.

See also **Drug Interdiction; Drug Laws, Prosecution of; Seizures of Drugs.**

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REVISED BY MARY CARVLIN (2001)

STRUCTURED CLINICAL INTERVIEW FOR DSM-IV (SCID). Structured Clinical Interview for *DSM-IV-TR* (SCID) is a diagnostic interview designed for use by mental health professionals. It assesses 33 of the more commonly occurring psychiatric disorders defined in the fourth edition text revision of the *Diagnostic and Statistical Manual* (*DSM-IV-TR*) of the American Psychiatric Association (2000). The SCID is a semi-structured interview that allows the experienced clinician to tailor questions to fit the patient's understanding; to ask additional questions that clarify ambiguities; to challenge inconsistencies; and to make clinical judgments about the seriousness of symptoms. The main uses of the SCID are for diagnostic evaluation, research, and the training of mental-health professionals.

The SCID is modeled on the standard clinical interview. It begins with an overview section that includes questions about basic demographic information (e.g., age, marital status), educational history, and work history, followed by questions about the chief complaint, past episodes of psychiatric disturbance, treatment history, and current functioning. The remainder of the interview is organized into the following sections: mood episodes, psychotic symptoms, differential diagnosis of psychotic disorders, differential diagnosis of mood disorders, substance-use disorders, anxiety disorders, somatoform disorders, eating disorders, and adjustment disorder. Although the substance use disorders (i.e., dependence and abuse) are assessed in a single section, the substance-induced disorders (i.e., substance-induced mood disorder, substance-induced psychotic disorder, and substance-induced anxiety disorder) are assessed in the mood, psychotic and anxiety disorder sections, respectively. Two optional modules, one for assessing suicidal thoughts and behavior (adapted from the Columbia Suicide-Severity Rating Scale) and one for assessing impulse control disorders, are also available. A separate interview, the Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders (SCID-II) is available for the assessment of personality disorders.

The SCID comes in three basic versions: the research version (known as the SCID-I-RV), the clinician version (SCID-CV), and a clinical trials version (SCID-CT). The research version contains the full complement of disorders, subtypes, and specifiers that are of interest to researchers. It is provided by the Biometrics Research Department at Columbia University as an unbound packet of

pages so that the investigator has the ability to leave out pages covering disorders or subtypes that are not relevant to a particular study. The bound clinician version (published by American Psychiatric Press) includes only those disorders and specifiers that are the most clinically relevant. The SCID-CT, designed specifically for clinical trials, provides customizable indication-specific configurations of the modules (e.g., for schizophrenia trials). A computer-assisted version of the SCID-CV is available from http://www.mhs.com, and a beta version of a computer-assisted SCID-RV is also available.

Training materials (e.g., didactic DVDs, DVDs of SCID interviews) can be ordered, and optional on-site training can be arranged. Additional detailed information about the SCID (including differences between the research and clinician versions, ordering information, training materials, reliability and validity references) is available on the SCID Web site (http://www.scid4.org).

Diagnostic criteria for substance dependence and abuse are assessed for eight classes of substances: Alcohol (ethanol), Sedative-Hypnotic-Anxiolytics, Cannabis (marijuana), Stimulants, Opioids, Cocaine, Hallucinogens/PCP, and Other (e.g., inhalants, atropine). For each class of substance, the interviewer determines whether the symptoms of dependence or abuse have ever been present during the subject's lifetime; whether they have been present during the last month; and the age when the first symptoms appeared. If dependence is current, the interviewer rates the current severity as mild, moderate, or severe. If dependence is in partial or full remission, the appropriate *DSM-IV-TR* remission specifier is noted (e.g., early partial remission, sustained full remission). Because alcohol use is so much more common than other substance use, the assessment for alcohol dependence and abuse is conducted first, followed by an assessment of dependence or abuse on the remaining categories of substances.

ALCOHOL SECTION

The alcohol section of the SCID begins with some overview questions about the subject's drinking history (e.g., "Has there ever been a period when you had five or more drinks on one occasion?" and "Has anyone ever objected to your drinking?"). The subject's answers to these initial questions allow the interviewer to sequence the assessment questions to match the subject's drinking history as follows: If a history of dependence seems likely (e.g., the subject reports a history of detoxification from alcohol or attendance at AA), the interviewer begins with the assessment of the individual *DSM-IV-TR* dependence criteria. (If criteria are met for dependence, the assessment of abuse is skipped since a *DSM-IV-TR* diagnosis of dependence preempts a diagnosis of abuse). If the history is not suggestive of dependence but is indicative of excessive drinking or problematic use, the interviewer commences with the individual *DSM-IV-TR* criteria for abuse. (If the criteria are met for abuse, the interviewer must then continue the assessment to see if the problematic drinking is sufficiently severe to qualify for dependence). Only if there have never been any episodes of excessive drinking and there is no evidence of alcohol-related problems can the interviewer skip the alcohol section and move on to the assessment of other substances.

DRUG SECTION

The drug section of the SCID is similarly structured to tailor the sequence of questions to the subject's drug-taking history. If, for any class of substance, the subject reports having used the substance on at least ten occasions in any one-month period, the interviewer starts with the assessment for dependence. If the subject reports using a substance at least twice, but less than ten times in any month, the assessment focuses on abuse. (As with the assessment for alcohol, if criteria are met for abuse, the interviewer follows up with the assessment for dependence). The interviewer checks for dependence on prescribed medications if the subject reports having been "hooked" on the medication or often taking more of it than was prescribed.

Two versions of the drug section are available: a standard version that assesses whether dependence or abuse has ever been met for any class of drug, and an alternate, more comprehensive version that assesses lifetime dependence and abuse for every class of drug ever used by the subject. In the standard version, the interviewer first determines which drug class has either caused the most problems or been used the most and then proceeds with assessing the criteria for lifetime dependence and/or abuse for

Reference (See Below)	Skre et al., 1991	Zanarini et al., 2000	Zanarini et al., 2000	Segal et al., 1995	Wiliams et al., 1992	Zanarini et al., 2001	Zanarini et al., 2001
Population Studied	N554	N527	N552	N540	N5592; Mixed Inpt, Outpt, Non-Pt.	N545	N530
Version of SCID	DSM-III-R	DSM-IV	DSM-IV	DSM-III-R	DSM-III-R	DSM-III-R	DSM-III-R
Design of Reliability Study	Joint; Audio-Tape	Joint; 84 Rater-Pairs from 4 sites	7–10 Day Interval Test-Retest	Joint; Audio-Tape	1–3 Week Interval Test-Retest	Joint; Observed Live	7–10 Day Interval Test-Retest
Major Depressive Disorder	.93	.80	.61	.90	.64	.90	.73
Dysthymic Disorder	.88	.76	.35	.53	.40	.91	.60
Bipolar Disorder	.79				.84		
Schizophrenia	.94				.65		
Alcohol Dependence/ Abuse	.96	1.0	.77		.75	1.0	
Other Substance Dependence/ Abuse	.85	1.0	.76		.84	.95	.77
Panic Disorder	.88	.65	.65	.80	.58	.88	.82
Social Phobia	.72	.63	.59		.47	.86	.53
OCD	.40	.57	.60		.59	.70	.42
GAD	.95	.63	.44		.56	.73	.63
PTSD	.77	.88	.78			1.0	1.0
Any Somatoform Disorder	2.03			.84			
Any Eating Disorder		.77	.64				

Notes: Values shown are for kappa, a measure of chance-corrected agreement.

SOURCE: (1) Segal DL, Kabacoff RI, Hersen M, Van Hasselt VB, Ryan CF. Update on the Reliability of Diagnosis in Older Psychiatric Outpatients Using the Structured Clinical Interview for DSM-III-R. *J of Clinical Geropsychology* 1995; 1:313–321 (2) Skre I, Onstad S, Torgersen S, Kringlen E. High interrater reliability for the Structured Clinical Interview for DSM-III-R Axis I (SCID-I). *Acta Psychiatr Scand* 1991 Aug; 84(2):167–73 (3) Williams JBW, Gibbon M, First MB, Spitzer RL, Davis M, Borus J, Howes MJ, Kane J, Pope HG, Rounsaville B, Wittchen H. The Structured Clinical Interview for DSM-III-R (SCID) II. Multi-site test-retest reliability. *Arch Gen Psychiatry*,1992; 49:630–636 (4) Zanarini MC, Frankenburg FR. Attainment and maintenance of reliability of axis I and axis II disorders over the course of a longitudinal study. *Comprehensive Psych* 2001 Sep–Oct 42(5):369–374 (5) Zanarini MC, Skodol AE, Bender D, Dolan R, Sanislow C, Schaefer E, Morey LC, Grilo CM, Shea MT, McGlashan TH, Gunderson JG. The Collaborative Longitudinal Personality Disorders Study: reliability of axis I and II diagnoses. *J Personal Disord* 2000 Winter; 14(4):291–9.

Table 1. Summary of selected SCID-I reliability studies. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

that class only. If criteria are not met for dependence or abuse on that class and there is evidence for problematic use of another class of drug, the interviewer next assesses dependence and abuse for that class of drug, continuing this process until the interviewer is satisfied that all relevant drug classes have been covered. In the alternate version, the interviewer makes ratings for every dependence and abuse item for each relevant drug class in parallel.

Table 1 summarizes the most comprehensive reliability studies of the SCID-I. Reliability for categorical constructs, such as the *DSM-IV* diagnoses being assessed by the SCID, is reported in terms of kappa, a statistic that corrects for chance agreement. Kappa values above 0.70 are considered to reflect good agreement; values from .50 to .70, fair agreement, and those below .50, poor agreement. As can be seen immediately in the table, the range of values of kappa from different studies and for different diagnoses is enormous. Many factors influence the reliability of an interview instrument such as the SCID, including study design (i.e., whether the reliability is joint interrater, in which the agreement is between raters observing the same interview versus the more stringent test-retest design in which two raters independently interview the same subject); interviewer training, subject population (i.e., better reliability is typically achieved using subjects with severe psychopathology as compared to subjects with milder psychopathology whose symptoms are more likely to be at the level of the diagnostic threshold), and disorder base rates (i.e., it is harder to obtain good reliability for rare disorders).

The validity of a diagnostic assessment technique is generally measured by determining the agreement between the diagnoses made by the assessment technique and some hypothetical "gold standard." Unfortunately, a gold standard for psychiatric diagnoses remains elusive. Perhaps the most accepted (albeit flawed) standard used in psychiatric diagnostic studies is known as a *best estimate diagnosis* in which the subject is diagnosed by a committee of experts using all available data.

Several studies (e.g., Ramirez Basco et al., 2000; Fennig et al., 1996; Kranzler et al., 1996) compared the SCID to best estimate diagnoses and demonstrated superior validity of the SCID over standard clinical interviews at intake episode.

See also **Addiction: Concepts and Definitions; Complications: Mental Disorders; Epidemiology of Drug Abuse; International Classification of Diseases (ICD); Models of Alcoholism and Drug Abuse.**

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STUDENTS AGAINST DESTRUCTIVE DECISIONS (SADD).

In 1981, Robert Anastas, a health educator and hockey coach in Wayland, Massachusetts, stood helplessly by as two of his students died from injuries sustained in two separate alcohol-related traffic accidents. Anastas decided to act: He developed a fifteen-session high school course on driving while impaired. Rather than a curriculum focusing solely on the effects of alcohol while driving, he taught strategies for preventing driving after drinking, and he emphasized the legal consequences of getting caught while driving under the influence. In this sense, the curriculum was a significant departure from traditional driver-education approaches.

ORIGINS OF SADD AND ITS GOALS AND EFFECTS

Students who took Anastas's course reacted enthusiastically and formed an organization to reduce alcohol-related traffic deaths among their peers. They initially called the organization Students Against Driving Drunk (SADD) in order to focus attention on the act of drunk driving, not on the drivers themselves. An anecdote related by Peggy Mann (1983) captures SADD's approach and philosophy: When a student jokingly suggested that SADD involve the governor, Anastas replied, "I believe that if you dream it, it can be done," and when the governor became the honorary chairman of SADD, its motto became "If You Dream It, It Can Be Done." Within a year, chapters had been formed throughout Massachusetts and the program was gaining national attention.

Members of the early SADD chapters had a number of goals. They sought to raise awareness of impaired driving among students through the curriculum developed by Anastas. They also sought to change norms related to impaired driving. Because they realized that most of their peers did not think of drinking and driving as wrong or risky, they reasoned that changing these norms was an

important component of reducing impaired driving problems. As the students put it, they wanted to change the "drinking and driving is cool" image to another image: "Drinking and driving is dumb." Finally, students in the SADD chapters sought to stimulate discussion between high school students and their parents about drinking and driving. To meet this goal, they developed a "Contract for Life," which stipulated that a student would call a parent if he or she had been drinking or if the person responsible for driving had been drinking, and the parent, in turn, agreed to provide a ride or taxi fare.

SADD was significant in three important ways. First, it was among the earliest prevention programs to emphasize student leadership. Other programs had used peer educators or peer counselors trained and supervised by adults, but SADD chapters were run by students who planned activities and took responsibility for making them happen. Second, SADD was among the first youth programs to recognize the importance of norms in impaired-driving prevention. Earlier programs had emphasized education, attitude change, or scare tactics. Third, SADD was one of the first school-based prevention programs to venture outside the classroom. Although SADD had a curriculum, it also entailed extracurricular, community, and family involvement. In this sense, SADD was the first of the so-called comprehensive school-based prevention programs.

ORGANIZATION GROWTH

SADD's early growth was rapid. By the mid-1980s, there were SADD chapters in every state in the United States and in Europe. SADD received considerable media attention and was the only alcohol-prevention program ever to be the subject of a nationally broadcast made-for-television movie, *Contract for Life: The Bob Anastas Story* (1984).

SADD was also controversial. Some vocal critics argued that SADD's emphasis on preventing drinking and driving implicitly condoned drinking by young people. They were particularly concerned about the Contract for Life. They argued that by ensuring safe transportation, parents were communicating the message that drinking itself was not a problem. Similar charges were leveled at Safe Rides and other programs that provided sober transportation for youth. Anastas and others countered that although drinking itself *was* a problem, young people were dying from traffic crashes, not just from drinking.

This debate, which resulted in the refusal by some funding agencies to allow grant money to be used to support SADD chapters, continued throughout the 1980s. SADD was also subject to criticism because of its acceptance of funding from the alcoholic beverage industry. In 1989, SADD divorced itself from this source of funds. It also adopted a strong no-use message and amended its Contract for Life to emphasize its commitment to a drug- and alcohol-free lifestyle. The organization specifically disassociated itself from safe rides and designated driver programs. However, it continued to characterize itself as an "inclusive, not exclusive" organization, recognizing that teenagers make mistakes and should not be punished for them. Rather, it sought to "inform, educate, support and empower young people to make positive decisions in their lives."

Over the years, SADD evolved. Junior high school and college programs were added, as was an emphasis on seatbelt use. In 1997, in response to calls from its chapters, the organization amended its popular name to Students Against Destructive Decisions, incorporating in its mandate other such potentially destructive behaviors as underage drinking and drug use, teen suicide, violence, and irresponsible sexual behavior or drug use that might result in the contraction of diseases. In the early twenty-first century, SADD chapters focus primarily on education, awareness, and peer support activities on a range of issues surrounding risky behaviors. Additionally, several student safety clubs with similar approaches to those of SADD have emerged. Members of these clubs, like SADD members, encourage students to reach out to other students to reduce highway deaths.

The mission of SADD has evolved as well. It is no longer sufficient to "just say no" to drinking and driving. The twenty-first century organization focuses on other forms of positive peer pressure aimed at helping students of all ages to choose not to make destructive decisions regarding drug use, risky sexual behaviors, underage and binge drinking, school and community violence, driving while impaired in any way, dating and relationship

violence, teen depression, teen pregnancy, and teen suicide.

Since the mid-1980s, SADD has been an international organization. In 1988, information on chapter creation was sent to students in the Netherlands, France, China, Japan, Iran, Jamaica, Israel, Germany, Australia, and Africa. In 1989, SADD chapters were established in the Soviet Union. In 1995, the Pruesser Group released the first systematic study of the effectiveness of SADD activities on teen decision-making. The results indicated that "students at SADD schools were more likely to hold attitudes reflecting positive reasons as to why NOT to use alcohol."

In 2000, SADD's partnership with Liberty Mutual insurance company for the purpose of creating annual surveys had its first release, which focused on communication barriers between parents and youth, the differences in how parents view critical aspects of teens' lives, and the importance of effective communication between parents and their children about making positive choices and avoiding destructive decisions.

See also **Accidents and Injuries from Alcohol; Dramshop Liability Laws; Driving, Alcohol, and Drugs; Mothers Against Drunk Driving (MADD); Parent Movement, The.**

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SUBSTANCE ABUSE AND AIDS.

Acquired immunodeficiency syndrome (AIDS) is a life-threatening disease that results from severe damage to part of the body's cellular immune system, the defense system against opportunistic infections and some cancers. The disease is acquired (as opposed to genetic or hereditary) and presents a myriad of clinical manifestations (syndromes) that result from severe damage to the immune system. AIDS was first identified in 1981 among homosexual men in California and New York, and among illicit-injected-drug abusers in New York City. After 1981, the numbers and types of AIDS patients increased rapidly; it was diagnosed in millions of persons throughout the world. In the United States alone, the Centers for Disease Control (CDC) estimated in 2003 that 1.0 to 1.2 million persons in the United States were living with HIV infection.

In 2006, injecting drug use was the primary risk factor for 13 percent of known HIV/AIDS cases in the 33 U.S. states with confidential name based reporting. An additional 3 percent of cases

occurred among men who have sex with men and also inject illicit drugs (MSM-IDUs). An additional 33 percent of the HIV/AIDS cases occurred among high-risk heterosexuals (who reported heterosexual relationship with persons known to be HIV infected or at high risk for HIV infection). A substantial percentage of the "high-risk heterosexual" partners are injecting drug users, though the data on the actual percentage are limited. Thus, a best estimate would be that injecting drug use is associated with one-fourth to one-third of the cases of HIV and AIDS in the United States. HIV and AIDS have also been found among non-injecting drug users—such as persons who smoke crack cocaine—but surveillance data are not available on sexual transmission of HIV facilitated by non-injecting drug use.

CAUSE

AIDS is caused by a viral infection. In the United States, the virus is called human immunodeficiency virus (HIV); it is one of a group of viruses called retroviruses (so-called because they can make DNA copies of their RNA, the reverse of what typically occurs in animal cells). In 1983, French researchers discovered the virus, which they had linked to an outbreak of enlarged lymph nodes (one early sign of HIV infection) that had been reported among French male homosexuals. The French named it the lymphadenopathy-associated virus (LAV). In 1984, U.S. researchers isolated HIV from AIDS patients and named it human T-lymphotropic virus type III (HTLV-III). American investigators found a way to grow HIV in laboratories in large amounts, which led to the development of laboratory tests that detect HIV infection.

HIV gradually destroys certain white blood cells called T-helper lymphocytes or CD4+ cells. The loss of these cells results in the body's inability to control microbial organisms that the normal immune system controls easily. These infections are called opportunistic because they take advantage of damage to part of the immune system. A few select cancers are also frequently diagnosed, such as Kaposi's sarcoma, a cancer of blood vessels, which appears as purplish spots on the skin or mucous membranes.

SIGNS AND SYMPTOMS

Early HIV Infection. The natural history of HIV disease and the time intervals between clinical events vary greatly from individual to individual. The general course, however, is one of exposure to HIV, which leads to infection. Within a few weeks or months of infection, laboratory evidence of infection can be detected as the presence of virus in the blood (viremia) or the appearance of the p24 antigen. Antibodies to HIV are found in the blood and indicate that infection has occurred. Some patients develop flu-like symptoms resembling mononucleosis or peripheral nerve abnormalities that are self-limited. This first stage of HIV infection is called the acute retroviral syndrome. Most patients have no symptoms during this period.

Latency Period. Over the ensuing years of a second, or latency, period (1–15 or more years), laboratory evidence of a decreasing number of helper T-lymphocytes can be measured. As the helper T-lymphocyte count decreases, patients are more likely to develop such signs and symptoms as enlarged lymph glands, fatigue, unexplained fever, weight loss, diarrhea, and night sweats. At about the same time or later, patients develop opportunistic infections or cancers. The diagnosis of one of the opportunistic infections or cancers indicates that the patient has developed AIDS. Pneumocystis carinii pneumonia, a fungal infection of the lung, is the most common opportunistic infection among AIDS patients. Other opportunistic infections include candidiasis of the mouth (thrush), cryptococcal meningitis, amebiasis, and cryptosporidiosis. Tuberculosis is another serious infection that has become increasingly common because of the AIDS pandemic.

Late-Stage AIDS. Late-stage AIDS is usually marked by a sharp decline in the number of lymphocytes, followed by a rise in the number of opportunistic infections and cancers. Kaposi's sarcoma is the most common cancer among AIDS patients. Kaposi's sarcoma usually arises in the skin and looks like a bruise or an area of bruises, but it grows and spreads to the internal organs. Another common type of cancer in late-stage AIDS is a form of lymphoma, or a tumor of the lymphatic system. Patients with late-stage AIDS may also develop inflammations of the muscles, arthritis-like pain in the joints, and AIDS dementia complex. AIDS dementia complex is marked by loss of reasoning ability, apathy and loss of initiative, loss of memory, and unsteadiness or weakness in walking.

DIAGNOSIS AND TREATMENT

Infection with HIV can be diagnosed with a blood test measuring antibodies to the virus. Antibodies are proteins produced by certain white blood cells in response to injection. The HIV antibody test became widely available in 1985. An enzyme-linked immunosorbent assay (ELISA) test for the presence of HIV antibody is used as the first test for detecting HIV antibody. Positive ELISA results are then tested with a western blot assay for confirmation. The use of these tests by blood banks has virtually eliminated the chances of contracting infection from transfusions.

Although a cure or vaccine for AIDS had not been discovered as of 2008, three groups of antiviral drugs are used to treat HIV infection.

Nucleoside Analogues. These drugs work by interfering with the replication process of the HIV virus. They include zidovudine (ZDV, AZT), didanosine (ddI), zalcitabine (ddC), stavudine (d4T), and lamivudine (3TC).

Nonnucleoside Reverse Transcriptase Inhibitors. These drugs work by blocking the activities of the RNA and DNA in infected cells. They include nevirapine and delavirdine. The drawback of this group of drugs is that the virus quickly develops resistance to them.

Protease Inhibitors. These are considered the most potent antiviral drugs. They inhibit the viral proteinase enzyme, which results in noninfectious particles of virus. The protease inhibitors include saquinavir, ritonavir, indinavir, and nelfinavir.

These drugs were usually given in combinations of at least two and preferably three compounds. Triple combinations, including one of the protease inhibitors, are considered the most powerful antiviral regimens. All antiviral treatment regimens must be individualized to the patient.

Because HIV frequently develops resistance to these drugs, particularly if patients do not take their medications with great consistency, there is a continuing need for developing new drugs.

HIV TRANSMISSION

HIV can be transmitted from person to person in three ways: (1) by contact with infected blood or blood components; (2) through intimate sexual contact; and (3) from an infected pregnant mother to her fetus. Drug abusers commonly become infected by sharing needles, syringes, and other injecting paraphernalia; injecting substances—such as heroin, cocaine, and amphetamines—after an HIV-infected person uses the needle and syringe causes direct inoculation of HIV. The sharing of needles and syringes can be thought of as a microtransfusion.

Sexual contact is a common route of transmission from drug abusers to their sex partners (who can transmit the virus to other sex partners, other drug abusers, or to unborn children). Various noninjected drugs, including crack cocaine and alcohol, can increase the likelihood of engaging in unprotected sexual activities. This drug use facilitated sexual transmission of HIV is a growing problem in the United States. Health care workers have also been exposed to HIV through unprotected or accidental direct contact with blood of infected patients in healthcare settings.

The World Health Organization (WHO) estimated that there were approximately 40 million persons infected with HIV in 2006, with about 4 million new infections per year. Most of these cases are in sub-Saharan Africa. Injecting drug use is not yet a major mode of HIV transmission in sub-Saharan Africa, but approximately one-third of new HIV infections outside sub-Saharan Africa are associated with injecting drug use.

PREVENTION AMONG DRUG ABUSERS

Three different types of programs have been shown to be effective in reducing HIV transmission among injecting drug users.

Community Outreach. Injecting drug users need accurate information about HIV and AIDS in order to reduce their risk behavior. While mass media can play an important role in transmitting such information, community outreach programs can be highly effective in delivering information as well as personally encouraging drug users to change behavior and providing referrals to other needed services. These outreach programs typically use former drug users.

Legal Access to Sterile Injection Equipment. As the virus is transmitted through sharing of drug injection equipment, providing good access

to sterile injection equipment is critical to reducing HIV transmission among injecting drug users. Syringe exchange programs, in which drug users bring in used needles and syringes (potentially contaminated with HIV), and are then given new sterile needles and syringes in return have become the best known type of program for preventing HIV among injecting drug users. Large-scale syringe exchange programs have been effective in preventing HIV among drug injectors in many different countries. Syringe exchange programs can also provide a wide variety of other health and social services to drug users. Legal sales of needles and syringes through pharmacies is another method of reducing HIV transmission among drug injectors, and syringe exchange and pharmacy sales should be thought of as a complementary rather than an either/or choice for HIV prevention.

Methadone Maintenance Treatment (MMT). Persons who enter drug-abuse treatment usually greatly reduce their illicit drug use and therefore their risk of becoming infected with HIV through sharing needles and syringes. Methadone maintenance therapy has been shown to be an effective therapy for opiate addicts and has decreased HIV transmission among patients. Buprenophine has also been shown to be an effective treatment for narcotic addiction, though, with the exception of a few countries such as France, it has not as of 2008 been implemented on a scale large enough to affect HIV transmission. While drug abuse treatment, methadone and burprenorphine maintenance in particular, can be very effective in reducing illicit drug use, it should be considered as treatment but not cures for addiction. Certainly drug abuse treatment should be provided to everyone who needs it, but people also need to develop new treatments for addiction, particularly for cocaine and other stimulant addictions.

Comprehensive HIV Prevention Programming for Drug Users. No one type of HIV prevention programming for injecting drug users is perfect in that it will completely eliminate injection risk behavior. However, combinations of community outreach, legal access to sterile injection equipment, and drug abuse treatment have prevented HIV epidemics among drug injectors in many countries. There is no justification for not implementing such programs wherever there is a threat of HIV being transmitted among injecting drug users.

See also **Alcohol and AIDS; Complications: Route of Administration; Injecting Drug Users and HIV; Needle and Syringe Exchanges and HIV/AIDS.**

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SUBSTANCE-FREE HOUSING. *See* Alcohol- and Drug-Free Housing.

SUICIDE AND SUBSTANCE ABUSE.

Suicide is a major public health problem (Sher, 2004). With more than 30,000 annual victims, suicide is the eleventh leading cause of death in the United States. Nearly a million people around the world commit suicide every year. If every suicide affects at least six family members or friends, then every year in the world there would be about 6 million new survivors. An estimated 8 to 25 attempted suicides occur per every suicide death.

Alcohol and illicit drugs are involved in about 50 percent of all suicide attempts (Hesselbrock et al., 1988; Aharonovich et al., 2002; Conner & Duberstein, 2004; Sher, 2006; Sher et al., 2007). About 25 percent of completed suicides occur among individuals with alcoholism or drug abuse. Substance abuse among young adults is largely responsible for the increased suicide rates under age 30.

The relationship between substance abuse and suicidal behavior has been more extensively studied for alcoholism than for drug abuse. To evaluate this relationship, it is helpful to understand the statistical association between alcohol and drug abuse and suicide, to learn which substance abusers are at particular risk of attempting or committing suicide, and to appreciate how this knowledge may be used to prevent suicide.

SUBSTANCE ABUSE INCREASES SUICIDE RISK

Alcoholism and drug abuse are important risk factors for suicidal behavior (Fowler et al., 1986, Roy & Linnoila, 1986; Murphy & Wetzel, 1990, Murphy, 1992, Cornelius et al., 1996; Sher, 2006; Sher et al., 2007). It was suggested that lifetime mortality due to suicide in alcohol dependence is as high as 18 percent (Roy & Linnoila, 1986). However, Murphy and Wetzel reviewed the epidemiological literature and found that the lifetime risk of suicide among individuals with alcohol dependence treated in outpatient and inpatient settings was 2.2 percent and 3.4 percent, respectively (Murphy & Wetzel, 1990). Nonetheless, individuals with alcoholism have 60 to 120 times the suicide risk of the nonpsychiatrically ill population. Higher rates of suicide attempts among individuals with alcohol use disorders have also been reported. For example, in an urban community in the United States, 24 percent of subjects with alcoholism attempted suicide, as compared to 5 percent with other psychiatric diagnoses (Weissman et al., 1980). Forty percent of a sample of depressed subjects with alcoholism who were hospitalized had attempted suicide in the prior week, and 70 percent had attempted suicide at some point in their lives (Cornelius et al., 1996).

Suicides are not random; each occurs in a particular context. The association between specific psychiatric syndromes—such as depression or abuse of alcohol or drugs—and suicidal behavior has been studied by epidemiologists, clinicians, and neurobiologists. Since interviews with suicide completers are impossible, retrospective reviews of the circumstances predating suicides have been conducted. By using interviews of relatives and others familiar with the suicide victim, together with study of medical records, suicide notes, and coroner reports, a suicide case is subjected to a "psychologic autopsy" (Pouliot & De Leo, 2006). Factors that distinguish successful suicide cases from suicide attempters and substance abusers who have never attempted suicide are identified in the hope that differences in these factors may identify those at particular risk for attempted or completed suicide. A limitation of retrospective studies is termed *recall bias*: Informants may provide information about the suicide victim that is distorted by their attempt to explain the suicide event. Although written records and use of standardized methods to collect diagnostic information can reduce this bias, prospective studies are more reliable. However, prospective studies in the general population are not feasible because suicide is rare, occurring in only about 1 in 10,000 annually (Sher, 2004). Approximately 10 percent of suicide attempters, 15 percent of depressed people, and 3 percent of individuals with alcoholism eventually commit suicide (Murphy & Wetzel, 1990; Murphy, 1992; Sher, 2004; Sher et al., 2007). By prospective study of such high-risk groups, additional risk factors can be identified during a follow-up period.

A prospective study of Swedish military conscripts found that those who drank more than 20 drinks weekly had three times the death rate, prior to age 40, of light drinkers (Andreasson et al., 1988; Allebeck & Allgulander, 1990). Most of these premature deaths were due to suicide or accidents. Those who develop alcohol dependence or abuse are, together with drug abusers, at increased risk of death from accidents, liver disease, pancreatitis, respiratory disease, and other illnesses; however, suicide is among the most significant causes of death in both male and female substance abusers. U.S. and Swedish prospective studies, for example, showed that alcoholism increased the risk of suicide fourfold in men and twentyfold in women.

Next to depression, alcoholism and drug abuse are the psychiatric conditions most strongly associated with suicide attempts. In the U.S. Epidemiologic Catchment Area (ECA) Study, the risk of

suicide attempts was increased 41-fold by depression and 18-fold by alcoholism (Moscicki et al., 1992). While cocaine users had increased rates of suicide attempts, users of marijuana, sedative-hypnotics, and amphetamines did not.

Among completed suicides, the proportion of alcoholics or drug abusers is large. Prior to 1980, alcoholism accounted for about 20 to 35 percent, and drug abuse for less than 5 percent, of suicides in a variety of countries (Sher et al., 2007). In the San Diego Suicide Study, conducted in the early 1980s, well over 50 percent of 274 consecutive suicides had alcoholism or drug abuse or dependence (Fowler et al., 1986). Much of the increase in young-adult suicide rates since the 1960s is attributable to alcoholism and drug abuse or dependence.

RISK FACTORS FOR SUICIDE ATTEMPTS

Alcoholics and drug abusers frequently threaten to kill themselves. Many, particularly women and young adults, actually attempt it. Among alcoholics studied in the ECA communities, 32.5 percent had attempted suicide during a period of active alcoholism. In a group of treated opiate addicts, 17 percent had attempted suicide (Moscicki et al., 1992). This represents at least a fivefold increased frequency of suicide attempts compared to those among non-substance abusers.

Although only about 10 percent of substance abusers who attempt suicide die in a subsequent attempt, most substance abusers who commit suicide have attempted suicide at least once before (Rosen, 1976). Thus, a review of the risks of suicide attempts may guide the identification of those substance abusers at risk of suicidal death. The risk of attempting suicide by an individual with alcohol or drug abuse is increased by co-occurring depression, bipolar disorder, antisocial personality disorder (ASP), and a history of parental alcoholism.

Even among people who do not abuse alcohol or drugs, major depression increases the risk of attempting suicide. Major depression is itself 50 percent more common among alcoholics than nonalcoholics: It was found among 5 percent of male and 19 percent of female alcoholics living in the five ECA communities (Weissman et al., 1988). Subsequently, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) demonstrated positive and significant associations between most substance use disorders and mood and anxiety disorders (Grant et al., 2004; Compton et al., 2007; Hasin et al., 2007). It was shown that 12-month alcohol dependence was strongly and significantly associated with all 12-month substance use and psychiatric disorders, including depression controlling for sociodemographic characteristics (Hasin et al., 2007). Lifetime alcohol dependence comorbidity followed a similar pattern. Drug dependence was also associated with mood and anxiety disorders in the NESARC (Compton et al., 2007).

Depressive feelings (but not necessarily the syndrome of major depression) often motivate alcoholics and drug addicts to enter a treatment program (Sher et al., 2007). Typically 20 to 40 percent of alcoholics in such programs have had a period of major depression during their lifetime. While many people drink alcohol or use drugs such as cocaine to reduce feelings of depression, experiments show that consumption produces an initial state of euphoria, followed within a few hours by anxiety, depression, and enhanced suicide ideas. In addition to the acute effects of alcohol and drugs, which involve initial euphoria followed by dysphoria, the chronic effects of substance use appear to include a progressive worsening of mood. The latter may be the most relevant to suicide risk among substance abusers, together with the impulsivity associated with intoxication. Retrospective studies have found that depressive symptoms are more common among alcoholics who have made a suicide attempt.

Studies have found that alcoholism in a parent is associated with suicide attempts among alcoholics (Coryell et al., 1992). Depressed patients with a family history of alcoholism are at greater risk for suicidal behavior (Sher et al., 2005). In addition, ASP and drug abuse, which commonly occur in genetically predisposed males who develop alcoholism early in life, are associated with suicide attempts. Many clinicians have noted the repetitive high-risk behaviors of intravenous drug addicts, who often are quite aware that they may acquire infection or die by overdose with each injection. Overdoses occur more commonly among heroin addicts who have attempted suicide than among those who have not. Highly impulsive and aggressive alcoholics or drug abusers with ASP may be a subgroup at elevated risk of attempting suicide. Transient but intense

dysphoria (feeling unwell or unhappy), though not of sufficient scope or duration to meet criteria for major depression, may nonetheless increase this group's risk of attempting suicide.

Prospective studies have found that depression, anxiety, and histories of violence and legal problems were predictive of suicide attempts in previously nonsuicidal drug addicts. Retrospective studies of alcoholics and drug addicts have found that poor social supports, occupational losses, personal losses such as divorce, and other family problems increase their risk of making a suicide attempt. Landheim and colleagues (2006) have shown that a substance use disorder with duration of more than 15 years and an early onset (less than 18 years of age) were independently associated with being a suicide attempter after controlling for other psychiatric disorders.

RISK FACTORS FOR COMPLETED SUICIDE

Individuals who attempt and those who complete suicide have somewhat different demographic, clinical, and biological characteristics. For example, women are three times more likely than men to attempt suicide, whereas men are three times more likely to commit suicide. However, there are overlapping problems: Every suicide attempt may result in completed suicide. Clinicians should take very seriously any suicide attempt.

High percentages of suicide completers with alcoholism had major depression at the end of life (Aharonovich et al., 2002; Sher, 2006). Depressed people, particularly men, typically kill themselves in young adulthood. Among alcoholics, over 90 percent of suicides occur among men (Allebeck & Allgulander, 1990; Sher, 2006). In contrast to depressives, alcoholic men typically commit suicide in their fifth and sixth decades, usually following about 20 years of alcoholism. Men with depression, but not those with alcoholism, continue to be at elevated suicide risk beyond age 60. Drug abuse shortens the interval preceding suicide: In the San Diego Suicide Study, drug addicts committed suicide after an average of only nine years of heavy use (Fowler et al., 1986). They typically did so in young adulthood, which suggests that factors other than alcoholism may shorten the suicide risk period in this group. About three of four alcoholic suicides communicate their suicidal intent prior to their deaths. Thus, middle-aged male alcoholics and young polysubstance abusers, especially those who talk of suicide, are at high risk of suicide. Bipolar disorder, schizophrenia, and ASP are also associated with suicide in substance abusers.

Ongoing substance use makes suicide more likely. Nearly all alcoholic suicides occur among active drinkers, and alcohol consumption often immediately precedes the suicide (Murphy, 1992; Sher, 2006). The abstinent alcoholic is only partly protected from suicide, however. It is likely that impulsiveness and depression contribute to suicides among abstinent alcoholics.

What determines the timing of suicide among substance abusers? Substance abusers often accumulate interpersonal problems throughout their drinking or drug-use careers, but one-third of those who commit suicide sustain a major interpersonal disruption (such as separation or divorce) within the six weeks preceding their deaths (Conner & Duberstein, 2004). They often are unemployed, living alone, and unsupported by family and friends at the time of this final and most severe disruption. In contrast, only 3 percent of nonalcoholics with depression suffer such a loss in the period before they commit suicide. Beyond psychiatric diagnoses, the strongest indicator of suicide risk in substance abusers is such an interpersonal loss. Beyond these actual losses, anticipated losses, such as impending legal, financial, or physical demise, may also increase the risk of suicide among substance abusers. Among alcoholics, those who develop serious medical problems, such as liver disease, pancreatitis, or peptic ulcers, are also at higher risk of suicide.

Availability of alcohol and guns at home may contribute to suicide risk, especially in adolescents and young adults. Overall, 28.7 percent of U.S. adolescents reported easy availability of alcohol in the home, 24.3 percent reported availability of a gun in the home, and 10.2 percent reported availability of both alcohol and a gun in the home (Swahn et al., 2002).

CLINICAL FEATURES

Substance abusers who commit suicide often see a physician or are psychiatrically hospitalized in the months prior to their deaths (Murphy, 1992; Conner & Duberstein, 2004; Sher et al., 2007). Those who talk of suicide may be ambivalent about their

wish to die. They may thus be amenable to clinical interventions such as detoxification, substance-abuse rehabilitation, or psychiatric hospitalization. Conversely, those who take special precautions against discovery during a prior suicide attempt are much more likely to die in a subsequent suicide attempt.

A model of suicidal behavior among persons with alcoholism has been proposed by Conner and Duberstein (2004). Predisposing factors that are presumed to increase (moderate) risk for suicide among individuals with alcoholism are aggression/impulsivity and alcoholism severity, which represent predominantly externalizing constructs, and negative affect and hopelessness, which represent predominantly internalizing constructs. To *externalize* means to attribute inner conflicts or feelings to external circumstances or causes. To *internalize* means to take in and make an integral part of one's attitudes or beliefs. Major depressive episodes and stressful life events—particularly interpersonal difficulties—are conceptualized as precipitating factors. This model can probably also be applied to individuals with drug abuse.

PREVENTION

Prediction of those who will complete suicide remains poor in individual cases, even among high-risk groups such as substance abusers. Despite their high prevalence, alcoholism and drug abuse often go unrecognized by physicians and other health care professionals. People with psychiatric disorders, suicidal behavior, and/or substance abuse are frequently stigmatized. Even physicians and other health care professionals frequently have negative attitudes. This detrimental approach compromises dual diagnosis patient evaluations, treatment, and prognosis. Clinicians should be educated about a risk of suicidal behavior among individuals with substance abuse. Clinicians' recognition of alcohol and drug use disorders and of risk factors such as major depression that increase the risk of suicide may assist them in making preventive interventions. The substance abuser with active suicide plans or a recent suicide attempt may need hospitalization, detoxification, and/or rehabilitation designed to foster abstinence from alcohol and drugs of abuse. Firearms should be removed from the homes of substance abusers with active suicide ideation, especially adolescents and young adults. Treatments designed to enhance social supports and foster abstinence from alcohol and drugs, together with those directed at the resolution of major depression, often reduce the risk of suicide. Careful assessment of suicide risk and appropriate treatment of comorbid psychiatric and medical disorders may reduce suicidal behavior in patients with substance abuse.

See also **Accidents and Injuries from Alcohol; Accidents and Injuries from Drugs; Complications: Mental Disorders; Epidemiology of Drug Abuse; Social Costs of Alcohol and Drug Abuse.**

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MICHAEL J. BOHN
REVISED BY LEO SHER (2009)

SWEDEN. *See* **Nordic Countries (Denmark, Finland, Iceland, Norway, and Sweden).**

SYNAPSE, BRAIN. The term synapse is from the Greek word *synaptein*, for "juncture" or "fasten together," by way of the Latin *synapsis.* It refers to the specialized junction found between nerve cells. It was conceived by the British pioneer neurophysiologist Sir Charles Sherrington (1857–1952) to describe the then-novel microscopic observations that the "end-feet" of one neuron physically contacted, in an intimate manner, other neurons to which it was structurally connected. A similar point of connection between peripheral nerves and their targets is usually referred to as a *junction.*

Synapses in the brain (see Figures 1 and 2) are morphologically typed by several features (1) a dilation of the presynaptic terminal (nerve ending) that contains accumulations of synaptic vesicles in various sizes, shapes, and chemical reactivities; (2) mitochondria; (3) a specialized zone of modified thickness and electron opacity in the presynaptic membrane, in which a presynaptic grid is perforated to provide maximum access of transmitter-containing vesicles to the presumptive sites of transmitter release; and (4) a specialized zone of altered thickness and opacity in the postsynaptic membrane termed the *active zone* and believed to be the site of initial response.

The synaptic vesicles have been shown to contain the neurotransmitters by a series of extensive analyses of meticuously purified vesicles. The vesicles differ in their protein content and may include the transmitter's synthetic enzymes, as well

Figure 1. Synapse. The nerve ending from one neuron forms a junction, the synapse, with another neuron (the postsynaptic neuron). The synaptic junction is actually a small space, sometimes called the synaptic cleft. Neurotransmitter molecules are synthesized by enzymes in the nerve terminal, stored in vesicles, and released into the synaptic cleft when an electrical impulse invades the nerve terminal. The electrical impulse originates in the neuronal cell body and travels down the axon. The released neurotransmitter combines with receptors on postsynaptic neurons, which are then activated. To terminate neurotransmission, transporters remove the neurotransmitter from the synaptic cleft by pumping it back into the nerve terminal that released it. (Modified from Figure 1, in M.J. Kuhar's Introduction to Neurotransmitters and Neuroreceptors in *Quantitative Imaging*, edited by J.J. Frost and H.N. Wagner. Raven Press, New York, 1990.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

as the transporters that can concentrate the transmitter within the vesicles. For monoamine neurons, the vesicles also contain specific proteins (named for their sites of discovery in the adrenal medulla as *chromogranins* but now termed more generally *secretogranins*. These are assumed to facilitate storage and release. Superficially, synapses with a thinner postsynaptic specialization, of about the same thickness as that at the presynaptic membrane (hence termed *symmetrical*), are often inhibitory; those with a thickened postsynaptic membrane (*asymmetrical*) are often excitatory.

Monoaminergic synapses, however, are often asymmetrical, as are those for peptide-containing neurons that do not obey these simple physiological categorizations. Synapses can also be discriminated on the basis of the pairs of neuronal structures that come together at this site of functional transmission. Most typical is the *axo-dendritic* synapse in which the axon of the presynaptic neuron contacts either the smooth or spiny surface of the dendrite of the post-synaptic neuron. A second common form is the *axo-somatic* synapse in which the presynaptic axon contacts the surface of the post-synaptic neuron's cell body (or somata). Less frequently observed are axo-axonic relationships in which one axon contacts a second axon-terminal that is in its own axo-dendritic relationship; such triads of axo-axo-dendritic synapses are found most frequently in spinal cord and certain midbrain structures, in which channels of information flow are necessarily highly constrained. Most rarely, junctions between cell bodies (somato-somatic) and dendrites (dendro-dendritic) have also been described.

The nature of the proteins that provide for the thickened appearances of the active zones by electron microscopy are not completely known, but

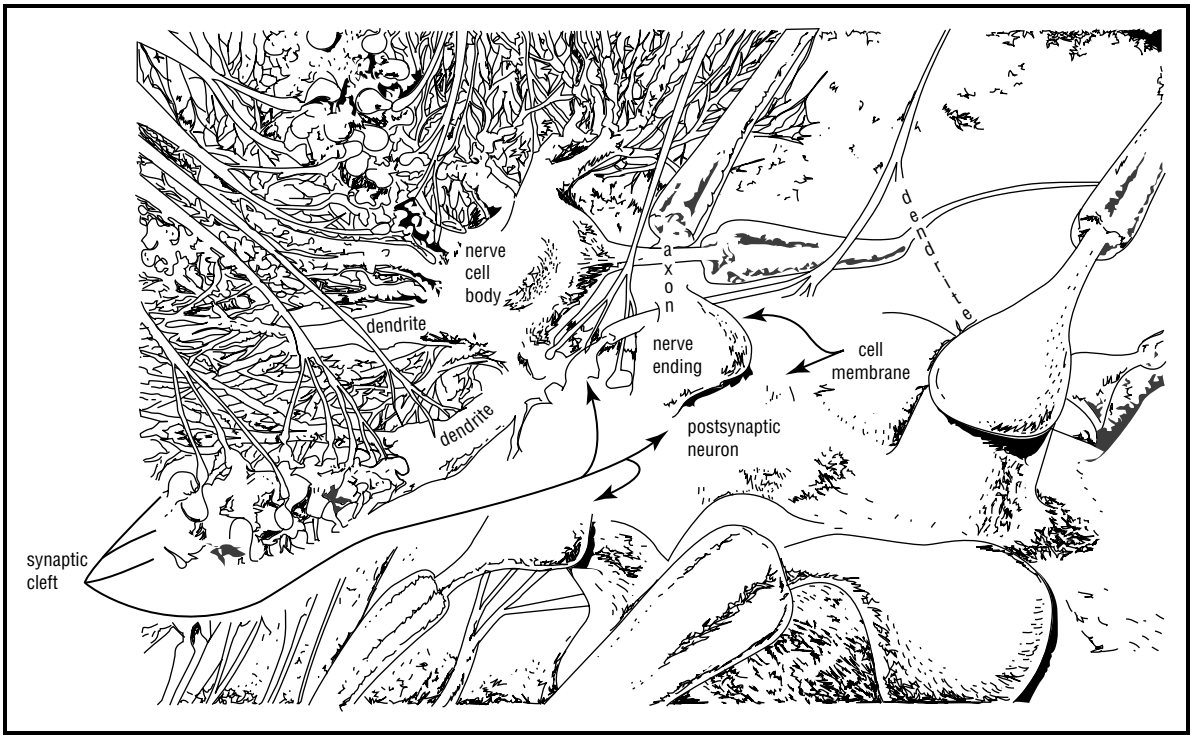

Figure 2. Neuronal complexity. The complexity of the neuronal network in the brain is demonstrated by this bundle of neurons, which form a vast and ramified structure with their cell bodies, outgrowths, and intercellular contact points. (Modified from Figure 1, in M.J. Kuhar's Introduction to Neurotransmitters and Neuroreceptors in *Quantitative Imaging*, edited by J.J. Frost and H.N. Wagner. Raven Press, New York, 1990.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

they include the postsynaptic receptors and associated molecules that can transduce the signals from the activate receptors, as well as those molecules that serve to concentrate the receptors in such locations.

See also **Brain Structures and Drugs; Neurotransmission; Reward Pathways and Drugs.**

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FLOYD BLOOM

T-ACE. T-ACE is a screening test for risky drinking by pregnant women. Heavy maternal drinking is a major pregnancy risk and a significant public health problem. Fetal alcohol syndrome (FAS) was first reported as a recognizable clinical syndrome nearly thirty years ago. It is characterized by:

1. prenatal and/or postnatal growth restriction
2. central nervous system (brain) abnormalities and
3. facial dysmorphology, i.e., an abnormal appearing face characterized by underdevelopment of the midface with small eyes, a short nose and a long simple (flat) philtrum, the area below the nose and above the upper lip.

As these children grow up, they are often mildly mentally retarded, with average IQs of about 70 and disabling behavioral abnormalities. In addition, there is a continuum of abnormalities among offspring exposed before birth to alcohol, but without the full syndrome abnormalities that are much more common than full FAS. There are anatomic anomalies, called alcohol-related birth defects (ARBD) and alcohol-related neurobehavioral disorder (ARND), a set of behavioral abnormalities in offspring prenatally exposed to substantial levels of alcohol. Other adverse pregnancy outcomes related to maternal drinking during pregnancy include miscarriage and stillbirth.

A national goal to reduce the prevalence of FAS by one half by decreasing maternal drinking was set in Healthy People 2000. Unfortunately, the reported prevalence did not decrease through the 1990s but in fact increased, possibly because of improved case finding. Regardless, it is likely that heavy drinking in pregnancy did not decrease, despite warning labels required on all alcoholic beverages since 1989.

There is evidence that pregnant women are receptive to advice from their health care providers, particularly their physicians, to quit or at least cut down on both drinking alcohol and smoking cigarettes. Given that such generalized warnings as the warning label have not proven effective, a more focused approach would seem reasonable—this would focus prevention efforts on women who drink or are likely to drink enough during pregnancy to damage their offspring. Such drinking has been labeled *risk drinking*.

The precise level of drinking that might damage the embryo/fetus is unknown, but is probably variable because of differing susceptibility and differing exposures depending on exactly which adverse effect is considered and when during pregnancy the exposure occurs (critical period). Solid estimates of risk drinking have decreased over the years, as better interviewing and statistical techniques have become available. It is now reasonable to use a figure of about seven drinks per week, typically massed on one or two days, but averaging about one drink per day or 0.5 ounces of absolute alcohol per day. This is the amount of absolute alcohol in one can of beer, one glass of wine or one mixed drink of standard size. This amount of alcohol intake, while unlikely to pose any health risk to the mother, is enough to adversely affect

	Question	+ Answer	Score
T	How many drinks can you hold (TOLERANCE)?	> = 6	2
A	Have people ANNOYED you by criticizing your drinking?	Yes	1
C	Have you felt you ought to CUT DOWN on your drinking?	Yes	1
E	Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (EYE-OPENER)?	Yes	1

The Tolerance Question is positive if the patient admits that she can hold, i.e., not get sick or lose consciousness, at least a sixpack of beer, a bottle of wine, or six standard drinks. As in the old song, (T) for two and two for (T) and, as in blackjack, each ACE is worth one. A total score of two or more is positive.

Table 1. The T-ACE Questionnaire. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

the embryo/fetus. There is not convincing evidence of clinically important effects on the offspring from an occasional drink during pregnancy.

There are, as of yet, no laboratory tests, i.e., biological markers, which will reliably identify at risk women. The only way to identify them is to obtain an appropriate history of drinking, but this is complicated by denial—the woman doesn't want to admit drinking to herself or to her doctor. Further, time is distinctly limited during prenatal visits and there are many problems to identify and address. Thus, a brief, simple questionnaire was needed. Most brief questionnaires, such as the CAGE, were developed and tested almost entirely in male populations, and do not function well for reproductive-age women.

The T-ACE questions were developed specifically as a screening test for risky drinking. They have been tested and validated over the last decade in women of multiple ethnicities, including white, African American and Native American, and across a range of socioeconomic statuses and geographic locations. The original questionnaire included the question, "How many drinks does it take to make you feel *high*?" as the (T)olerance question. An answer of greater than two standard drinks was considered positive. Several studies have now shown that substituting the *hold* question, included in Table 1, instead of the *high* question, gives better results, improving the sensitivity of the T-ACE questions.

T-ACE is a screening test, so it was designed to pick up as high a proportion of risky drinkers as possible. This version picks up about nine in ten women who drink enough in pregnancy potentially to damage their baby. If the score is less than two, i.e., the T-ACE is negative, it will correctly identify about seven in ten women who are not risky drinkers. It has a substantial false positive rate, i.e., warning the clinician, though the patient is not, in fact, a risk drinker. It has been speculated, though, that any woman who scores positive might, in fact, be at risk to drink too much during pregnancy and should be counseled.

Screening for risky drinking is not enough. At the minimum a brief intervention to support the patient in becoming abstinent during pregnancy or at the minimum cutting way down is warranted, as is close follow-up. If alcohol abuse or dependence is present, consultation or referral may be warranted.

See also **Fetal Alcohol Syndrome; Pregnancy and Drug Dependence.**

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ROBERT J. SOKOL

TAX LAWS AND ALCOHOL. The first internal revenue measure adopted by the U.S. Congress, in 1790, was an excise tax on domestic whiskey; a subsequent increase in that tax from 9 to 25 cents per gallon led to an armed insurrection by the farmers of western Pennsylvania during the summer of 1794, the so-called Whiskey Rebellion.

This matter of the appropriate level for alcoholic beverage taxes has remained contentious into the early 2000s; although there is consensus that alcoholic beverages should be subject to higher taxes than other commodities, substantial disagreement remains concerning the appropriate level for such taxes. The principal impetus for raising tax rates has always been the quest for increased government revenue. Since the 1970s, however, increasing attention has been paid to the public health benefits and societal costs savings of alcohol taxes, as research has demonstrated that raising the excise tax rates, and hence the prices of alcoholic beverages, reduces traffic fatalities and other costly consequences of alcohol abuse.

HISTORY

Alcoholic beverage taxes were a major source of revenues for the federal government throughout much of U.S. history. In 1907, this source accounted for 80 percent of federal internal tax collections and was still as high as 10 percent on the eve of U.S. entry into World War II. As of 2008, the federal excise taxes and import duties continued to have a considerable effect on the prices of alcoholic beverages, but figured very lightly (less than 1%) in overall federal tax collections.

Because federal excise taxes are set in dollar terms per unit of liquid, rather than as a percentage of the price, inflation gradually erodes the real value of these taxes. For example, while Congress increased the tax per fifth of 80-proof spirits by 29 percent (to $2.16) between 1951 and 2007, the overall level of consumer prices increased by over 550 percent during this same period. The result is that the real value of the federal liquor tax has declined substantially over time. By 2006 tax revenues that accounted for 12 percent of the sales in alcohol in 1980 amounted to just 7 percent of total sales. A considerable reduction in the average price of whiskey and other spirits relative to the prices of other commodities has been the inevitable result. Had the tax kept pace with inflation since 1965, the current $18 per-barrel tax on beer would total approximately $61.60, or $1.05 per six-pack, more than two-and-one-half times the current rate.

The states also impose special excise taxes on alcoholic beverages, as do some local governments. In addition, alcoholic beverages are generally subject to state and local sales taxes. The relative importance of these tax collections in state budgets differs widely, but as of 2006 it was less than 10 percent of government revenues everywhere. Between 2000 and 2008, however, 10 states raised excise taxes on alcohol.

TAX EFFECTS

When a legislature raises the excise tax rates on alcoholic beverages, the resulting cost to distributors is passed along to consumers in the form of higher prices. As is true for other commodities, the sales of alcoholic beverages tend to fall when prices increase. This is not to say that price is all that matters. For example, the steady decline in sales and consumption of alcohol during the 1980s cannot be explained by increased prices, since the prices of alcoholic beverages remained more or less constant (in real terms) during this period. The downward trend in consumption presumably resulted from the aging of the population and increasing public concern with healthy lifestyles, among other factors. Per capita sales and consumption of alcohol are nevertheless negatively affected by alcohol beverage prices, and if Congress had increased federal excise taxes substantially during the 1980s, sales would have declined still more rapidly than they did.

Although they differ somewhat, a number of published estimates of the price elasticity of demand for beer, wine, and liquor tend to confirm that price is one of the important variables influencing sales. One review of these estimates concluded that the price elasticity for liquor is approximately -1.0; this implies that, other things being equal, a percentage increase in the average price of liquor will result in an equal percentage reduction in the quantity of liquor sold. Beer and wine sales tend to be somewhat less responsive to price, with estimated price elasticities in the neighborhood of -0.5 (Leung & Phelps, 1993). Estimates for other developed countries are quite consistent with these conclusions (Edwards et al., 1994; Cook & Moore, 2000).

These results do not in themselves imply that a general price increase for alcoholic beverages will reduce consumption of ethyl alcohol (ethanol), the intoxicating substance in all these beverages. In the face of higher prices, consumers can switch to higher-proof brands, reduce wastage, and attempt home production of beer or wine. But in practice, research suggests that these substitutions are not large enough to negate the price effect. Ethanol consumption does tend to fall in response to a general increase in the price of alcoholic beverages.

Given the fact that higher alcohol excise taxes increase prices and reduce ethanol consumption, there remains the vital question of whether alcohol taxes are effective instruments in preventing alcohol-related harms. Of public concern are both the harms associated with the acute effects of inebriation—injuries stemming from accidents and violent crime—and the harms resulting from chronic heavy drinking, most notably the long-term deterioration in health and productivity.

There is considerable evidence that the incidence of both inebriation and chronic heavy drinking, and the associated harms, are sensitive to the prices of alcoholic beverages. For the acute effects, Cook (1981) studied 39 instances in which states increased their liquor tax between 1960 and 1975, finding strong evidence that traffic fatalities in those states fell as a result. This result was confirmed for the beer excise tax by Ruhm (1996) and Saffer and Grossman (1987), both using panel data on state traffic fatality rates. Cook and Moore (1993), also using panel data on states, found a close link between per capita ethanol consumption and violent crime rates, and direct evidence that an increase in the beer tax helped suppress rape and robbery. And Chesson and colleagues (2000) used a similar method to demonstrate that the incidence of sexually transmitted disease is inversely related to the beer tax. This literature is not without dissenters (see Dee, 1999), but the bulk of the published research results provides support for the conclusion that alcohol excises influence the incidence of inebriation and the costly consequences thereof.

There is also evidence of a link between alcohol prices and the prevalence of chronic heavy drinking. Cook and Tauchen (1982) demonstrated that changes in state liquor taxes had a statistically discernible effect on the mortality rate from cirrhosis of the liver. Since a large percentage of liver cirrhosis deaths result from many years of heavy drinking, it appears that chronic heavy drinkers are quite responsive to the price of alcohol. This conclusion is supported by evidence from clinical experiments and other sources (Vuchinich & Tucker, 1988).

Thus, there is indeed evidence that alcohol taxes are an effective instrument for preventing alcohol-related harms. The claim that alcohol taxes promote the public health is increasingly important in the public debate over raising federal and state alcohol taxes.

FAIRNESS

Although alcohol taxes reduce consumption and save some lives that would otherwise be lost to alcohol-related accidents, there remains the question of whether they are fair. Fairness is largely in the eye of the beholder (or taxpayer); nevertheless, several standards are commonly used as bases for judging the fairness of a tax. Two of the most notable standards are that a tax should fall equally on households which are in some sense equally situated and that it should not be regressive.

If equals are to be treated equally, is it fair that alcohol taxes force drinkers to pay more taxes than nondrinkers of similar incomes? Indeed, the bulk of all alcohol taxes are paid by the small minority who drink heavily: Half of all alcohol consumption is accounted for by just 6 or 7 percent of the adult population and 20 percent of drinkers consume 85 percent of all alcoholic beverages. One response is that it is fair for drinkers to pay more because drinking imposes costs on others. One estimate suggests that drinkers impose an average cost on others amounting to about 25 cents per drink (Manning et al., 1991); Miller and colleagues (1998) provide a much higher estimate. Thus, if the alcohol tax is considered a sort of *user fee*, whereby the drinker pays in proportion to the amount of alcohol consumed, then it may seem fair.

Another concern is that alcohol taxes may be regressive, meaning that on the average, wealthier households spend a smaller fraction of their income on alcohol taxes than poorer households. Although it is often taken as self-evident in political debates over raising beer taxes, the evidence on this matter is not clear (Sammartino, 1990; Cook & Moore, 1993).

Another debated issue is that of uniform taxation. A can of beer, a glass of wine, and a shot of spirits all contain approximately the same amount of ethanol, but are taxed quite differently; the federal excise tax on a shot of spirits exceeds the tax on a can of beer by a factor of 2, and on a glass of wine by a factor of 3. If special taxes on alcoholic beverages are ultimately justified by the fact that such beverages are intoxicating, then these disparities are difficult to explain. Part of the explanation may be the widespread belief that spirits are in some sense more intoxicating than beer or wine, and hence more subject to abuse, whereas beer is the *drink of moderation* and wine the *drink of connoisseurs*. But much of the evidence works against this view. Indeed, beer consumption may be more costly to society (per drink) than spirits because of the demographics of beverage choice: Young men—a group that consumes most of their ethanol in the form of beer—have by far the highest incidence of alcohol-related traffic accidents and violent crimes.

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TEA. Tea is the most widely consumed beverage in the world except for water, and provides over 40 percent of the world's dietary caffeine. In the United States, caffeine from tea accounts for about

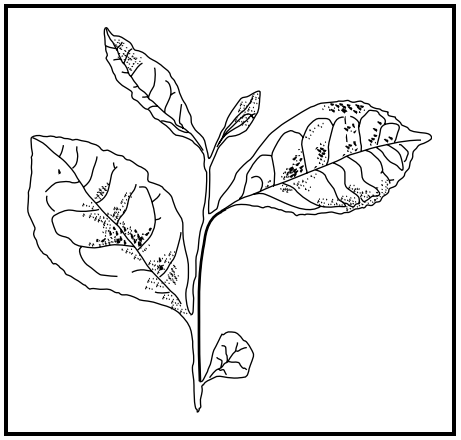

Figure 1. Tea leaf. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

17 percent of caffeine consumed; per capita caffeine consumption from tea is about 35 milligrams per day, which is a little over one-third of the daily caffeine provided by coffee beverages. Tea consumption in the United Kingdom is substantially higher, averaging 320 milligrams per capita per day and accounting for 72 percent of the United Kingdom's caffeine consumption.

Although tea contains a large number of chemical compounds, the relatively high content of polyphenols and caffeine is responsible for tea's pharmacological effects. The primary psychoactive component of tea is caffeine. Tea also contains two compounds that are structurally related to caffeine, theophylline and theobromine, however, these compounds are found in relatively insignificant amounts. On average, a 6-ounce (177-milliliter) cup of leaf or bag tea contains about 48 milligrams of caffeine, a little less than half the caffeine in the same amount of ground roasted coffee, and only slightly more than the amount found in 12 ounces of a typical cola soft drink. Six ounces of instant tea contain 36 milligrams of caffeine, on average. Individual servings of tea contain amounts of caffeine that can affect the mood and performance of adult humans.

Although the term *tea* has been used to refer to extracts from a large number of plants, only teas derived from leaves of *Camellia sinensis* plants are of special interest here, because they contain caffeine. The term *tea* has come to be used especially for extracts of *Camellia sinensis* and that restricted usage is maintained in this entry.

Consumption of *Camellia sinensis* was first documented in China (where tea is called *cha* or *chai*) in 350 CE, although there is some suggestion that the Chinese consumed tea as early as 2700 BCE. Tea was introduced to Japan around 600 CE but did not become widely used there until the 1400s. Through the China trade, tea became available in England in the 1600s, where it became the national drink. Tea was introduced into the American colonies around 1650 but in 1773 became a symbol of British rule. Americans protested the British tax on tea by raiding ships anchored in Boston harbor and dumping boxes of tea into the water. This event, referred to as the Boston Tea Party, along with other similar protests that followed, became important in shifting the predominant caffeinated beverage in North America from tea to coffee.

India, China, and Sri Lanka are the major producers and exporters tea—producing about 60 percent of the world's tea and providing about 55 percent of world tea exports. The United Kingdom, the United States, and Pakistan are the leading importers of tea.

Two types of tea, black and green tea, account for almost all the tea consumed in the world. Black tea makes up over 75 percent of the world's tea; green tea accounts for about 22 percent. The method by which tea is manufactured determines whether black or green tea is produced. Black tea is dark brown in color and is produced by promoting oxidation of a key tea constituent. Green tea is yellow-green in color and is produced by preventing such oxidation; it is therefore a less processed tea. Oolong tea, a less common type, is partially oxidized and is intermediate in appearance to that of black and green tea. Flavored teas were originally prepared by adding a range of fruits, flowers, and other plant substances to the tea prior to final packaging, although artificial flavors are often added today.

See also **Chocolate; Plants, Drugs From.**

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TEENS AND DRUG USE. *See* **Adolescents and Drug Use.**

TEMPERANCE MOVEMENT. Many temperance movements and societies emerged in the United States during the nineteenth century. These movements began in the early 1800s and gained ascendancy during the mid-to-late 1800s, culminating in the prohibition movement, the prohibition-banning Eighteenth Amendment (Article 18) to the U.S. Constitution in 1919, and the start of prohibition in 1920. Joseph Gusfield, an eminent scholar of the temperance movement, has argued that the term *temperance* is not appropriate because the broad reformist ideology of the movement focused mainly on abstinence—not moderation—in the intake of alcoholic beverages (1986). Jack S. Blocker observed that the many temperance movements that emerged in the United States represented men and women from varying ethnic, religious, social, economic, and political groups who selected temperance as the solution to what they perceived as problems in their own lives and in those of others (1989). By the end of the nineteenth century, the temperance movement had evolved through several phases, characterized by differences in goals and memberships (Murdock, 1998). Proponents changed their strategies from persuasive efforts to moderate the intake of alcoholic beverages to more coercive strategies, even legislation, to bring about the control of all drinking.

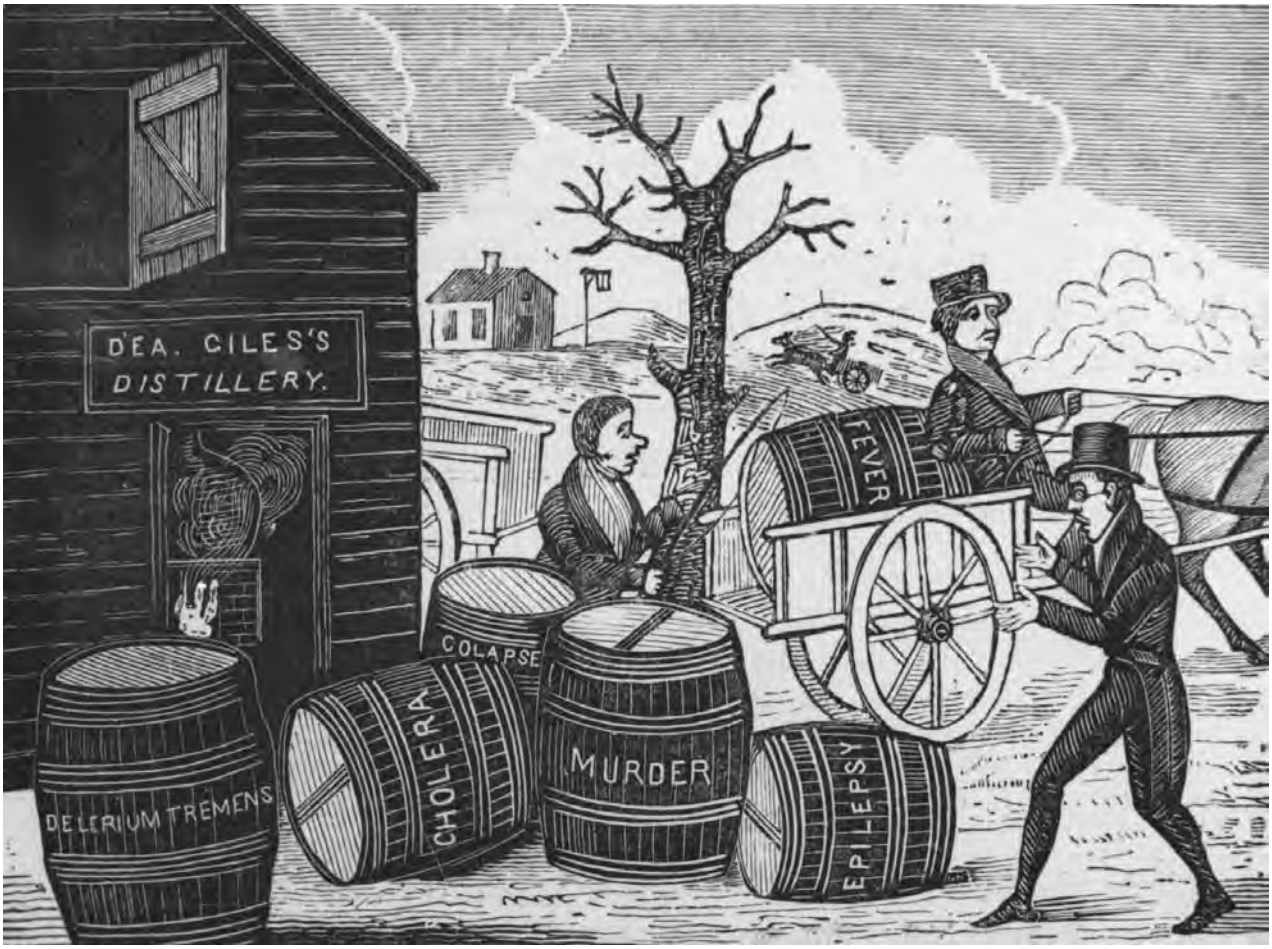
EARLY PHASE: 1800–1840

In colonial America and during the early 1800s, alcoholic beverages (brewed, fermented, and distilled) were a staple of the American diet, were often homemade, and were viewed as "the good creature of God" (Gusfield, 1986). Among the colonists, the drinking of alcoholic beverages was integrated with social norms; all social groups and ages drank alcoholic beverages, and the consumption rate was very high (Gusfield, 1986). Alcohol was also traded, sold, and given to Native Americans, who had no long history of daily drinking, with almost immediate negative consequences for these peoples.

By 1840, a revolution in U.S. social attitudes had occurred, in which alcohol came to be seen as "the root of all evil" and the cause of the major problems of the early republic, such as the crime, poverty, immorality, and insanity of the Jacksonian era (Tyrrell, 1979). Temperance was advocated as the ideal solution for these problems by such people as Anthony Benezet, a popular Quaker reformer; Thomas Jefferson; and Benjamin Rush, the surgeon general of the Continental Army and a signer of the Declaration of Independence. Temperance-reform organizations, such as the American Temperance Society, emerged, committed to the eradication of these social problems.

The American Temperance Society (ATS), founded in Boston in 1826 as the American Society for the Promotion of Temperance, was the first national (as opposed to local) temperance organization. It had its roots in the processes of industrialization and the commercialization of agriculture. The people who developed the movement were committed to hastening the processes of economic and social change. These processes involved the educating of Americans to value sobriety and industry in order to create the conditions for the development of an industrial-commercial society. The movement was supported by entrepreneurs who needed a disciplined and sober workforce to help create the economic change necessary for the material improvement of the young republic.

During the Second Great Awakening, from the early 1800s until late 1830s—a period of revivalism and evangelical fervor—the evangelical clergy, as well as that of other U.S. Protestant groups, supported temperance as a means of promoting the morality needed for building a "Christian nation," through social and economic progress. According to Gusfield, these groups helped to place the issue of drinking on the public and political agenda,



Woodcut of a political cartoon showing the evils of drink, c. 1820. © BETTMANN/CORBIS.

providing their personnel as authorities on the cognitive aspects of drinking and becoming the legitimate source of public policies on drinking (1986). Also, in the early 1820s and 1830s, small-scale farmers and rural groups were active in promoting the temperance movement. They saw temperance as a way to promote social progress in a time of transition from a rural to an urban-industrial order, from small-scale farming to entrepreneurial forms of agriculture.

By 1836, more than 200,000 people belonged to the American Temperance Society (ATS), which had become an abstinence society, and ideas about problems associated with alcohol had begun to change: Inebriety or habitual drunkenness was being called a disease. The ideology of the movement placed the source of alcohol addiction in the substance itself: Alcohol was inherently addicting, a finding supported by research conducted by the medical doctor, Benjamin Rush, who in 1785 wrote *Inquiry into the Effects of Ardent Spirits upon the Human Body and Mind* (Rose, 1996). Blocker observed that the general focus of ATS was on persuading the already temperate to become abstinent rather than persuading drunkards to reform their drinking behavior (1989). According to Gusfield, abstinence became a symbol that enabled society to distinguish the industrious, steady American worker from other people, which resulted in the movement becoming democratized instead of associated only with the New England upper classes (1986). Attempts to reform and save drunkards was the focus of another temperance movement, the Washingtonians (Blumberg with Pittman, 1991).

MIDDLE PHASE: 1840–1860

Whereas well-to-do groups and Protestant evangelical clergy dominated the early phase of temperance

reform, the middle phase included the efforts of artisans and women of the lower and lower-middle classes, who promoted self-help groups among largely working-class drunkards trying to give up drinking (Tyrrell, 1979). These artisans organized into the Washingtonian societies (named for George Washington), dedicated to helping working-class drunkards who were trying to reform.

In 1840, the first Washingtonian Temperance Society was established in Baltimore, Maryland. Members took a pledge against the use of all alcoholic beverages and attempted to convert drunkards to the pledge of *teetotalism* (c. 1834, derived from total + total = abstinence). By the end of 1841, Washingtonian societies were active in Baltimore, Boston, New York, and other areas throughout the North. These groups were not socially homogeneous. Tyrrell reported that the relationships between the old organizations and the new societies culminated in various struggles for control over the Washingtonian societies, with fragmentation of these groups occurring (1979).

Washingtonian members who wanted respect from the middle-class temperance reformers, including the evangelical reformers, elected to remain with the mainstream temperance movement. The wage earners and reformed drunkards remained in their own societies, and they opposed early efforts at legal coercion; for example, the passage of the Maine Law of 1851. Gusfield interpreted support for this law as a reaction against the drinking practices of the Irish and German immigrants to the United States between 1845 and 1855 (1986). He argued that temperance reform in this period represented a "symbolic crusade" to impose existing cultural values on immigrant groups. Tyrell (1979) interpreted the Maine Law as a way for middle-class reformers to control and reform the laboring poor. From 1851 on, many local laws were passed that attempted to limit the consumption of alcohol; however, throughout the remainder of the century, these statutes were repealed, liberalized, or not enforced.

LATE PHASE: 1860–1920

The Civil War, World War I, and the rapid demographic changes that accompanied immigration during this period contributed to the support of abstinence during the last phase of the temperance movements. Urban areas were expanding, factory towns were a reality, and there was an increase in the socializing at the end of the workday as well as at the end of the workweek; consequently there was an increase in the production and consumption of alcoholic beverages. Several temperance societies that emerged during this period included the active participation of women and children, as wives and children were often neglected or abused by drunken husbands and fathers. Irish-American Catholics formed the Catholic Total Abstention Union in 1872; the Women's Christian Temperance Union (WCTU) was formed in 1874; and the Anti-Saloon League of America (ASLA) emerged in 1896. These societies were able to mobilize tremendous support for abstinence rather than mere moderation in the intake of alcoholic beverages. During these years, the ideology of the temperance movements centered upon the evil effects of all alcohol, espousing the view that alcohol had become the central problem in American life and that abstinence was the only solution for this problem (Drowne, 2005).

The WCTU was the largest women's movement of the nineteenth century and the first mainstream temperance organization to involve women and children (Blocker et al., 2003). Its creative and dynamic leaders were Annie Wittenmeyer, Frances Willard, and Carrie Nation, who also supported the feminist movement, a radical movement at the time. The WCTU began a crusade to shut down saloons and promote morality. By the late 1870s the major theme of the temperance movement was the push for legal controls on drinking. The WCTU exists into the twenty-first century and is based in Evanston, Illinois; it lists about 12,000 members in the United States, and 20,000 worldwide as of 2008 (B. Wilson, personal communication, February 14, 2008).

By the late 1800s, coercive reform became the dominant theme of the temperance movement. In l893, the Anti-Saloon League of Ohio was organized by Howard H. Russell, a Congregational minister and temperance activist. In l895, this group combined with a similar group in the District of Columbia, establishing a national society in 1896: ASLA. By the end of the 1800s, the ASLA, which represented a skillful political leadership resource for the prohibition movement, mobilized tremendous support for abstinence instead of just

temperance. In 1896, the movement began to separate itself from a number of economic and social reforms, concentrating on the struggle of traditional rural Protestant society against developing urban systems and industrialization.

Part of the success of the ASLA was its determination to remain a single-issue (prohibition) pressure group that cut across all political party lines; the ASLA also maintained a strong relationship with the Protestant clergy. It always put its own issue first but worked peacefully with the major political parties and especially with legislators (Blocker et al., 2003). By 1912, local prohibition laws had been passed to render most of the South legally dry.

In 1917, a major event boosted the cause of national prohibition. The United States entered World War I, which prompted the ASLA to push for the suspension of the industrial distilling of alcohol (ethanol). Very shortly after the U.S. entered into the war, the selling of liquor near military bases and to servicemen in uniform was prohibited (Blocker, 1989). By 1918, the Eighteenth Amendment to the U.S. Constitution had been proposed and the ASLA had pushed prohibition through thirty-three state legislatures. Consequently, the Volstead Act—called Prohibition—was ratified on January 16, 1919. It went into effect one year later, on January 16, 1920, prohibiting the manufacture, sale, or transportation of alcoholic beverages.

TEMPERANCE MOVEMENT: IN HISTORICAL CONTEXT

Where the temperance movement was a middle-class reform movement, because it articulated the theme of self-control that was central to the middle-class ideology of the nineteenth century, some members of the working class also supported reform (Blocker, 1989). An ideology of abstinence became a rallying point for middle-class people who saw the rich as greedy, the working class as increasingly restless, and the poor as uneducated immigrants. Thus participants in the movement felt the need to restore a coherent moral order, especially after the upheaval of the Civil War and the ensuing period of industrial greed. At this time, the United States was undergoing economic expansion and deepening division along class lines. Other reform groups, such as the Progressive. Party, joined the prohibitionists in their commitment to rid cities of saloons so that the United States could move toward becoming a virtuous and moral republic. At the end of the nineteenth century, Americans seemed to be more receptive to moral than to scientific arguments for temperance reform and abstinence from alcohol.

Members of the temperance movements were concerned not only with changing the behavior of other social classes and groups but also about changing themselves (Levine, 1978). They were concerned that the pernicious effects of alcohol were also destroying the lives of people in the Protestant middle class. While some of these reform groups were not complete supporters of an abstinence ideology, they were concerned with rebuilding a national community and promoting the common welfare. Abstinence became the governing ideology of the many diverse groups that had mobilized to promote a new social order.

As more scholars turn their attention to the study of the temperance era and the various temperance movements and societies, additional knowledge and interpretations will be published. For example, Fletcher (2007), Mattingly (1998), and Rose (1996) observed that the biggest supporters of temperance have been women, a fact ignored by many scholars. Blocker and colleagues (2003) noted interests in literary criticisms and interpretations of temperance in the early twenty-first century that have the potential to create a broader and international field of study.

See also **Woman's Christian Temperance Union.**

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PHYLLIS A. LANGTON

TERRORISM AND DRUGS. The links between terrorism and drugs have evolved in relation to the shifting power dynamics of various struggles that have taken place in the Cold War between the free market and Communist state-controlled economies. All sides used terror in this struggle. And narcotics played a key role in sustaining paramilitary and terrorist organizations.

The dynamics of terrorism and drugs are a phenomenon of the late twentieth century, when developing countries assumed control of the means of production to both grow and distribute illicit substances. The main destination of the products is the West, with the financial proceeds from such transactions partially used to suppress armed struggle in the areas where the drugs are grown, and also used by insurrectionist organizations to fund their own terrorist campaigns. An inherent symbiosis exists between the grower and the principal areas of consumption, Western nations. The West is involved in two contradictory ways: in stimulating the trade as consumers and in prohibiting it through national and international policy. The effects on the developing world have been spiraling rates of intravenous (IV) substance use—coupled with poor support services—creating high rates of HIV. Both public health and governance in poorer nations suffer as narcotics money based on an illicit economy corrupts civil life.

In order to understand what led to the growth of terrorism and drugs, it is necessary to examine the genealogy of narcotics distribution. Prior to World War II it was primarily the nation-state and private entrepreneurs in Great Britain, Germany, and the United States that were responsible for trade in narcotic drugs. Between the two world wars Holland and Japan took the lead in the manufacture and distribution of psychoactive drugs, particularly cocaine. Given that narcotics use was widely practiced throughout all sectors of all societies apart from prohibitionist Japan until World War I when international prohibition began to take effect, the emergence in the developing world of the local warlord whose activities were financed by trafficking in heroin and cocaine is a latter-day phenomenon.

The shaping factors of Cold War politics and the rise of independent anticolonial movements, coupled with increased prohibition and enhanced forms of communication and travel, have created new forms of distribution. Cocaine and heroin can no longer be sold openly, as they were in the 1890s when Britain dominated international trade with its "tea" clippers and steamships. The international prohibition of narcotics, which included the Chinese Communist Party's suppression of opium production from 1949 to 1955 and a similar mandate by the Shah of Iran in 1955, meant that no nation-state could openly traffic in narcotics. It has now been left to various terrorist groups in the developing world to grow, manufacture, and distribute illicit drugs.

VIETNAM

The first group to draw on heroin as a commodity to fund an armed struggle was the Hmong hill tribe of Vietnam and Laos. The Hmong were supported by the West in their armed conflicts with the majority Khinh people of Vietnam who were Communist. The Hmong grew the poppies, harvested the opium, and with French support developed their own laboratories to transform opium into heroin. In return, they were able to buy weapons to maintain their armed struggle against the Viet Cong. Western security forces also ably assisted them in their drug distribution, most notably in Operation X. This involved flying opium from Laos to a French Special Forces Camp at Cap St. Jacques in South Vietnam, where it was sold to a consortium of Vietnamese gangsters, the Kuomintang (remnants of the KMT or Chinese Nationalist Party that remained in Southeast Asia rather than retreat to Taiwan), Corsicans, and various other brokers.

This strategy began with the French colonial effort to control the Vietnamese nationalist movement, the Viet Minh. It ended with the defeat of the French at Dien Bien Phu in 1954 where, ironically, the Viet Cong were aided by Hmong tribesmen who helped guide them through the jungle. This particular Hmong clan had become embittered toward the French because the latter, instead of dealing directly with tribespeople, had instead appointed Thai overlords to act as intermediaries. This action had driven down drug prices for the Hmong as the Thai overlords, drawn from another ethnic group, took a percentage of the profits. Following France's devastating defeat in 1954, the United States assumed control of French intelligence and, as documented by a number of historians, continued to run the Southeast Asian drug connection through Cuban dictator Fulgencio Batista and American mobsters Meyer Lansky and Santo Trafficante, with socially and economically deprived U.S. urban neighborhoods as their destination marketplace.

Initially, the Hmong formed an alliance with the West to seek support for their autonomy apart from the powerful and dominant Khinh. The West viewed them as anti-Communist insurgents. In response, the Hmong built a guerrilla army backed by Western powers that operated in the mountainous jungle regions in the border country of North Vietnam. In the early twenty-first century they continue to engage in opium production, with their subsistence economy struggling to come to terms with the opening up of Vietnam to free-market economics.

MYANMAR

In 1962 a military junta led by General Ne Win installed itself in Myanmar (formerly known as Burma), and the Shan and Karen people in Myanmar became involved in an armed struggle against it. Both of these ethnic groups were able to utilize the sale of opium poppy to purchase guns and ammunition and fund their wars of terror against (or liberation from) the Burmese state. By the 1980s the Burmese rebels produced half of the world's opium supply. As of the early twenty-first century, the Burmese government has negotiated a number of agreements with Shan warlords to cease hostilities, with the latter group shifting from opium to amphetamine production. The warlords themselves were then able to openly enjoy the benefits of their financial empires. The use of amphetamines in its various forms was extensive in 2008 in Southeast Asia, thus creating a new form of revenue.

CHINA

The KMT has supported its clandestine operations against the Chinese Communist Party through opium production. Its main focus was to create an armed rebellion in Yunnan, an area of southeast China bordering Vietnam. Initially based in Burma, the KMT operation was forced to relocate in 1961 to northern Thailand, where it took over the Thai opium trade, hauling 90 percent of Burma's export to addicted populations across the world. In return, the KMT was able to finance a terrorist operation in Yunnan province throughout the 1960s and 1970s.

AFGHANISTAN

The 1978 coup by the Communist People's Democratic Party of Afghanistan precipitated a crisis from which that country has never recovered. The initial terrorist campaign against the educated Afghani elite evolved into a wider elimination of all forms of alleged opposition, which included religious leaders, trade unionists, and anyone who posed a threat as not directly connected to the

Communist Party. The terror inflicted by the Communists created a counter-reaction to escalating atrocities, with the military eventually revolting in 1979. The former Soviet Union continued to back the Communist regime, even though it had lost popular support, and the West supported the opposing freedom fighters, the mujahideen. The rebels were able to finance their campaign against the Soviets by selling opium and heroin, whose ultimate destination was the streets of London and Berlin, in return for armaments. Although the main markets for Afghani heroin were located in the West, Soviet troops, many of whom were exposed to the drug for the first time, frequently took their drug use back to their cities, towns, and villages. This has had a devastating effect on Russian youth, for whom treatment operations hardly exist and the risk of HIV infection has seriously increased. The heroin use and addiction of young men who were drafted into the military from rural areas echo back to the American military experience in Vietnam.

Eventually in 1989, through a war of terror undertaken by both sides, the Soviets withdrew from Afghanistan, shattered by their failure to annihilate the tribal warlords and leaving behind an estimated 1.5 million Afghanis dead. Subsequent to the Soviet withdrawal, the existing government infrastructure in Afghanistan began to unravel. In the resulting power vacuum the mujahideen and various warlords fought for control. The U.S. Central Intelligence Agency (CIA) backed Gulbudding Hekmatyar, leader of the Hezbi-Ismali guerrilla group, a proto-fascist or Islamist faction, who eventually became the most influential drug warlord in the region. The result was that the Islamist Taliban emerged triumphant, able to realize its vision of an Islamic state based on the Sharia (Islamic law as derived from the Qur'an). In order to bankroll Afghanistan's shattered economy, the Taliban initially stimulated the growth of opium and then became involved in opium suppression as it tried to unsuccessfully shed its international pariah status.

Afghanistan was deemed to be a safe haven for the extremist Al Qaeda movement post 9/11, and the response was a United States-backed invasion in 2002. The invasion has yet to stem the growth in opium poppy, with Helmand province nominally controlled by the British Army becoming the opium bed of the world. The devastation in Afghanistan has created a seismic shift throughout central Asia as opium and heroin have bankrolled wars in Chechnya, Georgia, Bosnia, Croatia, and Uzbekistan while also destabilizing Pakistan. This drug trade is controlled by elements of Al Qaeda, tribal gangs, criminal warlords, and Western intelligence services.

The result has been political chaos and turmoil, with terrorism and drugs manifesting themselves in all their differing forms, and ideological or religious beliefs driving laws enacted and actions taken to control trade routes. Differing ideological gangs have fought for control and also cooperated in alliances. The financial gains derived from the opium and heroin trade have created forms of ideological drift as groups engaged in armed struggle, based on religious and political ideology, recognized the potential profits involved in narcotics supply. These far outweigh the economic gains of armed insurrection, and this becomes a key conceptual point for understanding another aspect of terrorism and drugs. The ideologies have become recruiting slogans to attract young ideologues into organizations rooted in the cause of terror. The end result, however, are narcotics gangs based on fear—whose main aim is to claim the consumer benefits of the free market, including stimulating the growth of the international sex trade—rather than a struggle against capitalism.

COLOMBIA

The rise of various political groups in Colombia is a significant conundrum for the West. Colombia became the third largest recipient of U.S. aid following the Clinton administration's commitment to a $1.3 billion military aid package to the Colombian military with the stated aim of eradicating coca plantations. Within Colombia a number of armed groups continue to vie for political power, based on various ideologies rooted in the right as well as the left. All to varying degrees are involved in the cocaine trade: its cultivation, taxing of the growers, refinement or distribution of the product.

One of the most well-armed groups of the right is a paramilitary umbrella organization called the United Self-Defence Forces of Colombia (AUC). Paramilitary forces directly participate in

processing cocaine; they are also involved in its manufacture and distribution. They are able to sustain their power base through acts of terror directed against any group that challenges their hold over a defined geographical area. They coexist with the army, the police, and other state forces as they conduct terror against the Ejército de Liberación Nacional (ELN or National Liberation Army) and Fuerzas Armadas Revolucionarias de Colombia (FARC or Revolutionary Armed Forces of Colombia), two factions that wish to overthrow the Colombian state.

AUC has a special role, maintaining close links with the state but not directly funded by it. AUC is able to carry out terrorist campaigns and assassinations outside the rule of the law. Because it funds itself by drawing on a vital international commodity, the cocaine trade, AUC can exist outside of state support systems and remain unaccountable.

Plan Colombia, a United States–backed attempt to suppress drugs and terrorism, is primarily directed at groups who operate in the south of Colombia. This area is largely controlled by FARC. It is here that the war on terror—the overriding U.S. foreign policy post-9/11—conflates with the War on Drugs into the war against FARC. This group is engaged in an armed revolutionary struggle in which kidnapping, assassination, bank robberies, and extortion are viewed as strategies to raise finances and to inflict a terrorist campaign against its perceived adversaries, the state apparatus of control. Interestingly, the AUC has not been constrained by Plan Colombia and benefits from the intelligence and resources mobilized by the CIA in its wars on drugs and terror.

FARC is a group that has its origins in Cold War politics, rooted initially in Marxism, but there has been a shift to Bolivar populism as it has sought to increase peasant participation in its so-called liberation army, which also contains a significant proportion of female combatants. Bolivar populism, pioneered by Bolivian President Evo Morales, is a form of pragmatic socialism based on the Cuban model, with an emphasis on health clinics and classrooms for poor communities rather than traditional Marxist or Leninist policies based on ownership of the means of production and capture of the state. Bolivia, for example, has nationalized the oil and gas production industry, reversing the previous policy induced by the free-market economics of the International Monetary Fund (IMF). Morales has also increased the government's royalties by more than U.S. $1 billion a year. Thus far this money has been used to fund infrastructure projects that bolster popular support for the governing party as well as lift the poor out of absolute poverty. Correspondingly, he has ended credit agreements with the IMF and withdrawn from the World Bank dispute procedure, thereby lessening the chance of outside interference in Bolivia's internal affairs.

During the Cold War Marxist- and Leninist-based insurgency, groups were partially sustained by the resources of the former Soviet Union. FARC has demonstrated that even with the demise of the Soviet state, a guerrilla movement based on leftist ideology can sustain itself. In fact, FARC has consistently grown in numbers and in terms of its areas of geographical control since the official collapse of Communism.

FARC remains able to sustain its organization by taxing the cocaine growers, along with other commodities grown in the region, and also by becoming involved in cocaine distribution to middlemen who then create their own networks to distribute the drug across South America, North America, and Europe. The U.S. government's response to this trade has been the indictment of FARC leadership on charges of $25 billion worth of cocaine distribution. Until 2008 similar activities of AUC were ignored. Various official reports on drug distribution in Colombia, including one authored by Senator John Kerry in 1986, clearly indicated the complicity of the CIA in overriding the strategic aims of the Drug Enforcement Agency (DEA) to try to contain insurgency groups.

FARC was labeled as an important terrorist organization in the post-9/11 debates on U.S. security. American strategy has emphasized crop eradication as a way forward, strangling FARC's ability to raise finances. The debates surrounding the success of this form of intervention have revolved around what has had the most effect, the American aerial eradication strategy or the Colombian military approach based on manual eradication, or if the entire intervention has been counterproductive as FARC appears, to some observers, to have increased its hold. Each position is rooted within the ideology of the participants and is part

of a war of words, one intended to sap the morale of the opposing side and seek funds to continue various terrorist campaigns.

The IRA in Colombia. The arrest of three provisional Irish Republican Army (IRA) members in August 2001 in Colombia highlighted the links between FARC and other groups formerly engaged in wars against the state. The senior IRA members had travelled to Colombia to allegedly provide technical knowledge about bomb making to FARC. In return, FARC was to provide funds to assist the IRA in transitioning from an insurgency group to a legitimate political group. In their past struggles the IRA had consistently patrolled its areas of the Six Counties in Northern Ireland ensuring that drugs did not penetrate the Irish Catholic Housing Estates. Punishments were meted out to those involved in the distribution of marijuana; they ranged from warnings to banishment to kneecapping. Following the ceasefire with the U.K. government, the links forged through various armed confrontations coupled with the technical knowledge gained over a twenty-year struggle allowed certain members of the former IRA to gain consultancy roles with other insurgency groups. There is some dispute over whether this was the group's official policy or if the individuals involved had operated on their own. The IRA kept its sense of purpose intact throughout twenty years of insurgency largely through strict discipline. Deviation from the leadership's aims was never tolerated, so it is inconceivable to some that senior members would have decided to participate in a nonauthorized operation.

CLOSING REMARKS

Since the beginning of the twentieth century there has been a substantial shift from state distribution of narcotics to developing nations becoming involved in their supply. The proceeds of the sale of drugs have primarily fueled conflict within supply nations, and the examples here highlight the situation in Vietnam, Myanmar, Afghanistan, and Colombia. The latent effect is that groups wishing to further their interests must be able to finance their campaigns either for or against the state. The sale of drugs allows governments and insurgents to buy weapons. These proxy wars destabilize government systems, induce campaigns of terror, and encourage the growth of the narcotics industry and narcotics use. The situation has been exacerbated by the role of Western intelligence agencies that have drawn on these various groups, asking them to fight wars based on the agencies' interests, which could not be fought conventionally. The impact of these various strategies is significant: It has ensured that drugs have become integral to the flow of international capital and are intrinsically linked to the sex trade, the arms industry, and money laundering.

See also **Crop Control Policies; Foreign Policy and Drugs, United States; International Drug Supply Systems.**

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DEAN WHITTINGTON

TETRAHYDROCANNABINOL (THC).

Tetrahydrocannabinol, or THC, is a chemical found in the hemp plant, *Cannabis sativa*, that causes the psychoactive effects of marijuana, bhang, hashish, and ganja. Hashish is derived from the resin that oozes from the flowering tips of the female plant; bhang comes from the dried leaves and flowering shoots of the female plant; and ganja comes from small leaves. THC is one of the three natural cannabinoids—chemical constituents of *Cannabis*—the other two being cannabinol (CBN) and cannabidiol (CBD).

As of the early twenty-first century, marijuana is the most commonly used nonlegal drug in the United States. Its usage peaked during the late 1970s, when about 60 percent of high school seniors reported having tried marijuana, with 11 percent reporting daily use. Usage has declined since 1979; as of 2003, 5.1 million Americans aged 12 or older described themselves as daily users.

PHARMACOLOGICAL EFFECTS

For more than 30 years, the discovery of the mechanism of THC's action had eluded the best researchers. The problem seems finally to have been resolved by the detection of specific cannabinoid-binding sites (receptors) in the brain. A further step in unraveling the mechanism of THC's action has been the cloning of the cannabinoid receptor.

The pharmacological effects of THC vary with the dose, the method of administration, the user's degree of experience with THC, the setting, and the user's vulnerability to the psychoactive effects of the drug. Most users seek to experience a "high," or "mellowing out." The high begins about 10 to 20 minutes after smoking and lasts about 2 hours. The psychological effects obtained during the high are often related to the setting in which the drug is taken.

Inhalation. THC is most commonly taken into the body by inhaling the smoke from marijuana "joints." A joint of good quality contains about 500 milligrams of marijuana, which in turn contains between 5 and 15 milligrams of THC. Blood levels of THC rise almost as rapidly after inhaling smoke as they do after intravenous administration of THC. That the drug should be so rapidly absorbed is an indication of the efficiency of the lung as a trap for the drug. THC is quickly redistributed into other tissues so that blood levels decline over the course of 3 hours to negligible amounts. The usual symptoms of marijuana intoxication are almost completely gone by that time.

Ingestion. THC is absorbed slowly and unreliably from the gut after oral administration. Blood levels of the drug peak between 1 and 2 hours after ingestion. These peak concentrations are also considerably lower than those following smoking.

THC is easily soluble in fats. It is taken up and stored in the fatty tissues of the body and in the gray matter of the brain. This pattern of storage is one reason why THC remains so long in the body.

Withdrawal. THC does not produce a severe withdrawal syndrome. Heavy users, however, frequently report insomnia, nervousness, mild stomach upset, and achy muscles—particularly if they stop their use suddenly.

DRUG TESTING AND FORENSIC ISSUES

Drug testing is an issue with respect to marijuana because of the effects of THC on coordination, sense of timing, and impairment of depth perception as well as short-term memory. It is hazardous for someone who has taken a moderate dosage of marijuana to drive or to operate heavy equipment in the workplace.

Urine testing, however, is hardly useful for determining impairment, since the metabolic products of THC are detectable for as long as 50 days in chronic users. Urine tests are also of little use in determining the patient's pattern of use.

EFFECTS OF THC

THC produces a variety of complex sensations and behavioral effects in humans. The effects on memory, coordination, and sense of time have already been noted. Some studies indicate that THC produces impairment of human cognitive functions as well. In addition, many users experience increased appetite. Psychological effects range from a pleasant sense of mellowness to negative effects that include panic reactions, anxiety, hallucinations, and schizophrenic symptoms. THC can also cause relapses in schizophrenic patients, even those who are taking antipsychotic medications. These negative effects are more common with high doses of the drug and with oral ingestion rather than smoking.

The physical effects of THC include dry mouth, abnormalities in heart rhythm, and abnormal precancerous changes in the tissues that line the airway and the lungs. People who are heavy users of marijuana often develop bronchitis and laryngitis. As of the early twenty-first century it is known that persons who smoke only marijuana have an increased risk of lung cancer, as well as those who smoke tobacco. THC lowers the sperm count in males and may produce abnormal menstrual cycles in females. Women who are pregnant or nursing are advised to avoid marijuana, as THC is secreted in human breast milk.

MEDICAL USES OF THC

THC has been used in medicine to treat the nausea that many cancer patients experience after chemotherapy. It has also been used to prevent convulsions

and to lower the fluid pressure inside the eye in treating glaucoma.

In recent years, THC has been replaced in medical use by a synthetic derivative called dronabinol (Marinol). Dronabinol is used as an antinausea drug, an appetite stimulant in AIDS patients, and an antiglaucoma medication.

See also **Drug Metabolism; Drug Testing Methods and Clinical Interpretations of Test Results; Pharmacokinetics: General.**

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THEOBROMINE. This alkaloid belongs to the class of drugs called methylxanthines; it is similar to theophylline and to caffeine. Theobromine (3,7-dimethylxanthine), however, is somewhat weaker than these two compounds and currently has almost no practical use in medicine.

Theobromine is found in the seeds of the plant *Theobroma cacao*, which is the well-known source of chocolate and cocoa. The cacao seeds have caffeine too (as does tea, which contains small amounts of theobromine and theophylline). Caffeine has powerful stimulant effects on the brain, whereas theobromine has very little (although popular articles alleged for years that theobromine makes one feel "happy"). High doses of theobromine can, however, affect several physiological functions in the body, such as increasing the formation of urine in the kidney.

See also **Alkaloids; Caffeine; Chocolate.**

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MICHAEL J. KUHAR

TOBACCO

This entry includes the following essays:

A HISTORY OF TOBACCO

The term *tobacco* generally refers to the leaves and other parts of certain South American plants that were domesticated and used by Native Americans for the alkaloid nicotine. Tobacco plants are a species of the genus Nicotiana, belonging to the Solanaceae (nightshade) family, which also includes potatoes, tomatoes, eggplants, belladonna, and petunias. Including plants used for tobacco, there are 64 Nicotiana species. The two widely cultivated for use as tobacco are Nicotiana tabacum and

Nicotiana rustica, the latter of which contains the higher levels of nicotine.

Nicotiana tabacum is, however, the major source of commercial tobacco, although it has been hybridized with other Nicotiana species and its chemical composition altered in the process. Nicotiana tabacum is a broad-leaf plant that grows from three to ten feet (1–3m) tall and produces ten to twenty leaves radiating from a central stalk. Nicotiana rustica, also known as Indian tobacco, was first cultivated by Native Americans and was probably the tobacco offered to Columbus. The word *tobacco* came into English about 1565 from the Spanish word *tabaco*, which probably derives from the Taino word for the roll of leaves containing the N. rustica that the indigenous people of the Antilles smoked.

HISTORY OF TOBACCO USE IN EUROPE

Tobacco was introduced to Europeans by Native Americans at the time Columbus explored the New World (1492–1506). The first written records of tobacco use date from this time, but there is archaeological evidence for tobacco's wide use in the Americas as early as 600 to 900 CE. Native Americans considered tobacco to be sacred, and the plant was used in social, fertility, and spiritual rituals. For example, tobacco was used for seasonal ceremonies, for sealing friendships, preparing for war, predicting good weather or good fishing, planting, courting, consulting spirits, and preparing magical cures. The desired effect of tobacco was a trance state, achieved by using the leaves in various ways, including smoking, chewing, snuffing, drinking (tobacco juice or tea), licking, and injecting in enemas.

Tobacco Use Spread from the Americas to Europe. Acute nicotine poisoning was a central aspect of the practice of shamanism in many parts of South America. South American shamans would smoke or ingest tobacco to the point of producing a nicotine-mediated trance or coma. The dose of nicotine could be titrated to produce a coma state resembling death, but from which the shaman would recover. Recovery from apparent death was believed to enhance the perception of the shaman's magical powers.

Tobacco use spread widely through all the Americas, and most tribes had ceremonial traditions related to tobacco. Although tobacco ceremonies were common among native tribes in the Americas from Canada to Argentina, the traditions and stories about the origin of tobacco vary greatly. In 1492 Columbus encountered natives in Hispaniola smoking tobacco in the form of large cigars. Enticed by the sacred and special regard in which they held tobacco, Columbus's crew experimented with tobacco smoking and soon became enthusiastic users. In the early 1500s tobacco cultivation began in Portugal. By the late 1500s, France had introduced tobacco cultivation to Holland and later to Italy. By 1570 tobacco had been introduced to Germany, Switzerland, Austria, and Hungary. In central Europe tobacco was primarily used for medicinal purposes. Tobacco was said to be useful in the prevention of plague and as a cure for headache, asthma, gout, ulcers, scabies, labor pains, and even cancer.

Objections by James I to Tobacco. In 1570 the tobacco plant was named Nicotiana after Jean Nicot, the French ambassador to Portugal who introduced tobacco to France. In the late 1500s, Sir Walter Raleigh popularized the smoking of tobacco for pleasure in the court of Queen Elizabeth I (reigned 1558–1603); from there it spread to other parts of England.

James I of England (reigned 1603–1625), who succeeded Elizabeth, was strongly opposed to tobacco use and in 1604 wrote the first major anti-tobacco treatise, *A Counterblaste to Tobacco.* King James described tobacco as "a custome loathsome to the eye, hateful to the nose, harmful to the brain, dangerous to the lungs, and in the black stinking fume thereof nearest resembling the horrible stygian smoke of the pit that is bottomless." Despite James's opposition, however, tobacco use flourished. Eventually, even James lessened his opposition to tobacco because of the lucrative income from its taxation. Governments often became addicted to the tax revenues from tobacco much like people became addicted to the chemicals being taxed. These revenues were often used to fund wartime efforts and support the economy during desperate times (Courtwright, 2001, p. 156).

Throughout Europe pipe use became the popular method of consuming tobacco, and the first vending machine for pipe tobacco was introduced in England in 1610. During the Thirty Years War (1618–1648), which began as a struggle for

religious supremacy that grew into a large-scale non-religious struggle for political dominance in Europe, tobacco use expanded primarily through the ranks of warring armies. With Germany being the primary battle area for the war, historians estimate that nine out of every ten peasant homes had a tobacco user (Corti, 1932, p. 108). Also during this time, medical practitioners began treating many common ailments with tobacco, leading to increased use of the pipe.

Tobacco as Big Business, and Its Critics. In the early 1600s, Spain, Portugal, and England increased their financial investment in tobacco through cultivation in their North American territories. In 1614, King Phillip III of Spain declared Seville the tobacco center of the world and had all Spanish crops in the Americas funneled through Seville. Simultaneously, the English expanded cultivation in their colony of Virginia. In 1619, the first slaves arrived in Virginia to cultivate English tobacco crops. Rapidly expanding tobacco production by the English was credited for the slave trade industry in the seventeenth and eighteenth centuries. Tobacco growers in the Americas realized that growing tobacco required large numbers of permanent laborers and found inexpensive labor from the Africans being shipped from West Africa. Although many were originally brought to the Americas as indentured servants, the practice transformed into slavery as profit-minded plantation owners institutionalized the practice of owning permanent laborers and providing only for their basic needs plantation owners.

Throughout the 1600s increasing numbers of antismoking regulations spread throughout Europe and east to Russia. The Russian Czar Michael Feodorivich (1596–1645) declared tobacco use a deadly sin and established harsh punishments for offenders. Murad the Cruel of Turkey (1623–1640) ordered that tobacco users be beheaded, quartered, and/or hanged. As the anti-tobacco pressures increased in Europe and Russia, tobacco trade moved into Asia. By the mid-1600s, smoking was a pastime in China, Japan, Korea, and India. Shortly, antismoking pressures increased, leading Persia and India to enact death penalties for tobacco use. In 1620 Japan banned smoking for the first time. Nevertheless, smoking persisted. Government prohibitions became costly to national economies as the trade of tobacco moved to black markets. India's tobacco bans in the late 1800s alone created a significant negative impact on government revenue as tobacco revenue dropped from 14 percent in 1880 to 7 percent in 1905 (Courtwright, 2001, p. 183).

Due to the enormous profit in tobacco trade, smuggling and black markets for tobacco increased greatly during the 1700s. Ireland and Scotland became gateways for tobacco smuggling. Tobacco created an economic boom leading to population growth and prosperity in Glasgow. During the early 1700s, England's state of war with France and Spain contributed to Scotland and Ireland's prosperity in tobacco as their ports provided safer transport than England's.

Despite countervailing pressures, tobacco was also recognized as having medicinal properties. During an outbreak of the bubonic plague (Black Death) in England in the mid-1600s, tobacco was recognized as a preventive measure. Young men during this period were encouraged to smoke a daily pipe at Eton College and were routinely punished for not doing so.

Royal Support of Tobacco. During the 1700s, Europe saw a resurgence of tobacco use among European elites. Smoking had become primarily a pastime of the lower and middles classes following the Thirty Years War and the social elite turned to using tobacco in the form of snuff, a finely ground tobacco powder inhaled through the nose. Opposed to smoking, Louis XIV of France promulgated the use of snuff as a discreet habit that did not offend others with smoke. Snuff-taking throughout the 1700s increased dramatically. In contrast to most of Europe, Frederick I and Frederick William I of Prussia were avid pipe smokers who began the first tobacco club with the sole purpose of promoting smoking.

PRODUCTION OF CIGARETTES IN NORTH AMERICA

In France and England, snuff-taking continued to grow in popularity among the aristocracy. Even Napoleon I was rumored to consume up to seven pounds of snuff a month. Expensive to produce and package, snuff was used mostly by the upper classes. Snuff-taking was popular until the mid-1800s when smoking was reintroduced with the emergence of cigars from the Spanish colonies. Various ancestors

to the modern cigarette first appeared in the mid-seventeenth century. For example, the famed Casanova (1725–1798) in Italy helped popularize the hand-rolled cigarette. Not until 1843, however, did Manufacture Francaise des Tabacs produce the first commercial cigarette. Napoleon III (1808–1873) helped popularize the cigarette with his own 50-per-day habit. With the introduction of mass production of commercial cigarettes, large manufacturing plants began to appear in Europe and North America. In 1847 Phillip Morris opened his first production plant in England, producing hand-rolled Turkish cigarettes.

Tobacco production was a mainstay of American capitalism. In contrast to Europe, the U.S. public preferred chewing tobacco to smoking in the early 1800s. By 1860, the U.S. business census listed 348 tobacco factories producing chew tobacco in North Carolina and Virginia alone. However, cigar smoking also grew in popularity in the United States after soldiers in the Mexican War (1846–1848) returned with a desire for the darker, richer tobacco found in Latin cigars. Most tobacco was smoked as cigars or in pipes or used as snuff. Cigarettes were hand rolled. A skillful worker could roll four cigarettes per minute. Cigarette smokers were primarily boys or women, and smoking was a behavior confined to the lower socioeconomic class.

The gold rush of 1849 in California spurred an American interest in finer tobaccos and liquors. San Francisco became known as the capital for the *best bad things* in the United States. The Civil War contributed to the U.S. growth in tobacco consumption in two ways. First, the ration packs for soldiers in both the Confederate and Union armies contained tobacco products. Second, the U.S. government imposed the first excise tax on tobacco to help fund the Civil War for the Unionists.

Introduction of the match in 1852 and mass production of commercial cigarettes caused cigarette consumption to rise in the latter half of the 1800s. Increased smoking led to resurgence in antismoking regulations. In 1868, the British Parliament banned smoking on all commercial trains. In 1871, the U.S. House of Representatives voted to ban smoking in its own chambers. The U.S. Senate was able to enact the ban in its chamber in 1914. Nonetheless, smoking prevailed.

Cigarette Rolling Machine. The invention of the cigarette rolling machine by James Bonsack in 1880 made tobacco use inexpensive and convenient. Bonsack went into business with W. B. Duke and Sons in Durham, North Carolina. Together they improved the machine; by April 30, 1884, the device could roll 120,000 cigarettes per day. Duke used his competitive edge in manufacturing with an exclusive agreement with Bonsack to drive the price down, making cigarettes more affordable for the general public. Duke's American Tobacco Company dominated tobacco through the late 1800s but eventually collapsed in an anti-trust action in 1911.

Popular Culture and the Cigarette. By the late 1800s, tobacco had entered the world of popular entertainment and had begun to appear in popular fiction. Mérimée's 1865 novel about a cigarette girl in Seville became the basis for the opera *Carmen*. In 1878, trading cards and coupons began to appear in packs of cigarettes. Sports figures became the first trading cards to link tobacco and celebrity. By the beginning of the 1900s cigarette consumption in the United States had increased more than fourfold. At the same time, chewing tobacco had reached its peak consumption.

Ironically, as pressures increased in the U.S. Congress to ban or control tobacco, the government listed tobacco in the *U.S. Pharmacopoeia*. This government endorsement of tobacco as a medicinal agent led to partnerships between the tobacco companies and the medical community. In 1899, the first *Merck Manual*, a widely used reference book for physicians, listed tobacco as a treatment for bronchial distress and asthma.

Mass media opened doors to tobacco never experienced before the first half of the twentieth century. The glamorization of cigarette smoking increased through the use of entertainment celebrities as spokespersons and the inclusion of smoking in the new motion picture industry. Both world wars provided a venue for increasing tobacco use by soldiers, who received cigarettes as rations. Tobacco advertising also included doctors among the role models depicted as smoking cigarettes. Despite the fact that tobacco had been removed from the *U.S. Pharmacopeia* by 1905, smoking was considered sophisticated, glamorous, individualistic, and even healthful. Across the world, the average person was spending 3 to 5 percent of his or

her total income on tobacco by 1951, according to John B. Hutson, president of Tobacco Associates in a paper published in that same year.

HISTORY OF OPPOSITION TO TOBACCO USE

Strong opposition to tobacco consumption emerged by the turn of the twentieth century with 43 of the 45 states addressing tobacco as a menace. Business owners joined ranks in 1908 and began refusing employment for people who smoked. However, bans on sales of tobacco to minors were the only successful national regulation in the United States, Canada, and England. Despite antismoking regulations, tobacco consumption in the first half of the 1900s increased, peaking in 1955 in the United States with 50 percent of men smoking and in 1966 for women, with 32 percent of women smoking. By the 1960s nearly half of Americans were addicted to nicotine.

Health Hazards and Legal Action. While there had been occasional reports on the health hazards of cigarette smoking from the time of King James, the first large-scale studies documenting the link between cigarette smoking and cancer appeared in 1950 (Doll & Hill, 1950; Wynder & Graham, 1950). Subsequently, hundreds of studies have shown that cigarette smoking accounts for 30 percent of cancers—including some cancers of the lung, mouth, throat, esophagus, bladder, and kidney, as well as some leukemia; and that it is the cause of some heart and vascular disease, stroke, emphysema, chronic obstructive lung disease, and other health problems. The U.S. Office of the Surgeon General regularly publishes findings regarding the health consequences of tobacco use with the most comprehensive report released in 2004. The first comprehensive review of the scientific research regarding the health consequences for nonsmokers regularly exposed to smoke in their work, home, and social environments was published by the U.S. Office of the Surgeon General in 2006. This report has been paramount in supporting tobacco bans worldwide.

Unprecedented scientific and legal efforts to reduce the use of tobacco emerged in the second half of the twentieth century. With mounting support that tobacco causes different types of cancer, multiple lawsuits were filed in the 1950s in the United States against tobacco companies. The increase in scientific literature led to the 1962 report by the Royal College of Physicians in Britain and the 1964 Surgeon General's Report in the United States linking tobacco with lung cancer. The largest public health campaign related to any one issue began with these reports.

The 1960s in the United States started the era of comprehensive tobacco control. Regulations were passed that limited advertising by tobacco companies. Tobacco advertising on television was banned in the United Kingdom. Warning labels about the dangers of tobacco had to be placed on all tobacco products in the United States. The U.S. Surgeon General released three more reports on the dangers of smoking. By the 1970s legislation was introduced in the United States and the United Kingdom that banned smoking in public places, including airlines. Individual states within the United States began to draft legislation to control where people would be allowed to smoke.

During this same time, in stark contrast to many of the industrialized nations moving toward smoking bans, Japan stood out for its political support of smoking. Emperor Hirohito started a tradition of passing out cigarettes to all of his employees on his birthday. He also provided free cigarettes to the elderly on a holiday honoring them. Japan's consumption of tobacco peaked in 1966 with 84 percent of men smoking, according to the World Health Organization in 1998.

Federal Restrictions. In the 1990s the United States and other industrialized nations moved to reduce both the affordability and convenience of smoking. Federal and state governments began placing large taxes on tobacco products that significantly increased the cost of tobacco. With smoke-free laws being regulated, making smoking less convenient, more regular smokers quit. By the end of the 1990s, according to the Centers for Disease Control, smoking rates in the United States had dropped to about 25 percent in the adult population.

In 1997 the United States Attorney General's Office and the tobacco companies came to the largest agreement ever settled by the tobacco industry. The master settlement agreement severely restricted advertising, required bold warnings on tobacco, and limited damages against tobacco companies in lawsuits. The tobacco companies admitted they knew tobacco was addictive and company executives lied about the dangers of using tobacco.

Tobacco control efforts had mixed impact in Asia. In 2000, Japan demonstrated the effect of pressures to control tobacco use as Emperor Akihito repealed the tradition of handing out cigarettes to staff on his birthday. Smoking rates dropped to 47.7 percent that year. With all the tobacco control efforts across the globe during this time, China National Tobacco Company accounted for 31 percent of the tobacco market, representing 385 million smokers in China in 2000, making it the dominant tobacco trader in the world.

In February 2005 the Framework Convention on Tobacco Control (FCTC) took effect in the 40 countries that ratified it. The convention sought to protect the world's citizens from the dangers of secondhand smoke. By 2008 over 65 countries had established smoke-free laws that limit or ban smoking in public places. In the United States, according to the 2007 *Morbidity and Mortality Weekly Report*, rates dropped from 25 percent in 1999 to 21 percent in 2004. In the United States smoking rates among teenagers dropped from 28 percent in 1991 to 23 percent in 2005. Although the overall smoking rate dropped through the early years of the twenty-first century, the U.S. Centers for Disease Control reported a disproportionate number of smokers among African Americans, Asian Americans, and the gay/lesbian populations.

While smoking rates continued to drop in industrial nations, WHO noted that smoking rates in developing countries were on the increase in the early years of the twenty-first century. With the increased restrictions for marketing in industrial nations, the largest tobacco companies looked elsewhere for profits, developing multinational offices to increase marketing efforts in developing markets.

See also **Advertising and Tobacco Use; Nicotine; Nicotine Delivery Systems for Smoking Cessation.**

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AN INTERNATIONAL OVERVIEW

The tobacco plant (*Nicotiana tabacum*) is native to the western hemisphere where it has grown from 6000 BC to 3000 BC and was used by indigenous peoples for religious and medicinal purposes. Since the seventeenth century, the cultivation and use of tobacco has spread worldwide. By the early twenty-first century, tobacco had become an industry worth $400 billion in annual revenues. Around one in three adults uses tobacco.

PHARMACOLOGY OF TOBACCO AND ITS EFFECTS

Tobacco, in its natural form, contains over three thousand compounds. Its cultivation, processing, and manufacture into various products; combination with other compounds; and routes of delivery; in turn, result in differences in absorption into the body. Tobacco smoke, for instance, contains over five thousand known chemical compounds, including highly volatile gaseous and vapor components and larger smoke particles (tar). There are at least fifty carcinogens released when a cigarette is smoked, including benzene, formaldehyde, and hydrogen cyanide. Some compounds increase the addictive properties of smoking, alter behavioral patterns, or produce additional effects in the brain and central nervous system (CNS).

The key substance found in tobacco is nicotine, a liquid alkaloid first isolated in 1828 by German chemists Wilhelm Heinrich Posselt and Ludwig Reimann. Nicotine makes up about 0.6 to three percent of dry weight of tobacco. It readily diffuses through the skin, lungs, and mucous membranes (such as the lining of the nose or gums), with the amount absorbed dependent on the type of tobacco leaf, method of use, and specific product. For example, cigarettes contain eight to twenty milligrams of nicotine, of which around one milligram is absorbed when smoked. Smokeless tobacco products (snuff and chewing tobacco) deliver three to four times the amount of nicotine delivered by a cigarette, which is absorbed more slowly but remains in the bloodstream longer.

The most common and expedient way to get nicotine into the bloodstream is through inhalation. Alveoli (tiny air sacs in the lungs where gas exchange occurs) provide an enormous surface area for access by nicotine. Once in the bloodstream, nicotine travels to the brain, taking an average of seven seconds. The nicotine then acts upon two nicotinic acetylcholine receptors in the brain—a ganglion type nicotinic receptor and a CNS type nicotinic receptor—increasing their activity. By binding to ganglion type nicotinic receptors, the adrenal medulla increases the flow of adrenaline (epinephrine), a stimulating hormone. This, in turn, causes an increase in heart rate, blood pressure, and respiration, as well as higher blood glucose levels. By binding to CNS type nicotinic receptors, dopamine levels in the reward circuits of the brain are increased, generating feelings of pleasure similar to that caused by cocaine and other stimulants. Other chemical messengers released by nicotine are acetylcholine, norepinephrine, vasopressin, arginine, and endorphins (small proteins that are often called the body's natural painkiller).

For the user, the amount of specific chemical messengers released, and the resultant feelings they induce, depend on the level of nicotine in the bloodstream. If a smoker takes short quick puffs on a cigarette, this will produce a low level of blood nicotine. Low doses enhance the actions of norepinephrine and dopamine in the brain, causing a stimulating effect that increases alertness and

concentration. In contrast, deep puffs produce a high level of blood nicotine that enhances the effect of serotonin and opiate activity. This leads to an increase of acetylcholine and beta-endorphin, and a depression of the passage of nerve impulses. The result is a mild sedative effect, decreasing anxiety and producing a calming, even painkilling effect. Nicotine is thus unique in comparison to most drugs because its profile can change from stimulant to sedative/painkiller depending on dosage and use.

Nicotine has a half-life of one to two hours. The user must therefore self-dose with nicotine again to sustain its pharmacological effects. This repeated use is prompted by two further factors. First, tolerance develops over time so that users must absorb more nicotine to achieve the same effect, which explains how users can rapidly move to using increasing amounts of tobacco. Second, tobacco use leads to strong dependence or addiction. The pharmacological and behavioral characteristics that determine tobacco addiction are similar to those that determine addiction to such drugs as heroin and cocaine. While using nicotine-containing products, the body adapts the way it works to compensate for the effects of the nicotine. For example, neurons in the brain might increase or decrease the number of receptors or the amount of different neurotransmitters affected by the presence of nicotine. When there is no longer nicotine in the body, these physiological adaptations remain. The net result is that the body cannot function the same way in the absence of the drug as it did before, at least in the short term. Withdrawal symptoms include irritability, anxiety, depression and, above all, craving for nicotine. It is for this reason that, of the millions of people who try to stop smoking annually, only 10 percent succeed. In about a month, these feelings subside as physiological and psychological re-adaptation occurs.

SPREAD OF TOBACCO CULTIVATION

Tobacco was first cultivated by the peoples of the pre-Columbian Americas, with large-scale cultivation beginning in the sixteenth century. In 1527 the first tobacco plantation was established in Haiti by the Spanish. In 1612 John Rolfe raised the first commercial crop of wild tobacco (*Nicotiana rustica*) in the English colony of Jamestown, Virginia, founded by Sir Walter Raleigh, for export to England. Growers soon switched to common tobacco (*Nicotiana tabacum*), a milder variety with rapidly growing demand in Europe. Within seven years, tobacco became the most valuable cash crop of the day, without which the American colonies would have failed. As tobacco farming expanded throughout the colonies, growers brought British prisoners, debtors, and eventually African slaves to work on the plantations.

In 1492 the South American Arawak tribe gave Christopher Columbus dried tobacco leaves, which he took back to Europe along with seeds. It was not until the mid-sixteenth century, however, that tobacco became popularized in Europe by sailors, explorers, and diplomats, such as Sir Frances Drake, Jean Nicot (after whom nicotine is named), and Francisco Hernández de Toledo. By the 1600s, tobacco cultivation in Europe began to be established. Sir Walter Raleigh is attributed with establishing one of the first tobacco farms in England.

Tobacco was first introduced to the Middle East by the Turks who took it to Egypt in the early 1500s. It was introduced to China in the late 1500s via Japan and the Philippines, and in 1560 Portuguese and Spanish ships brought tobacco to East Africa where it then spread to Central and West Africa. Tobacco exports from South America to South Asia via Europe, through the British East India Trading Company and Dutch East Indies Company, commenced in the eighteenth century. This early trade arrived in eastern Mediterranean ports and was taken overland along the great Silk Road to Persia, Mughal, and China. The Portuguese colony of Goa was also supplied by sea. Under the Raj (1700–1800), widespread use of tobacco was established in South Asia, fuelled by an export drive by British merchants connected to the Virginian tobacco farmers. Initially smoked in pipes and hookahs, tobacco gradually became indigenized, mixed with local spices and additives to produce such products as *gutka*. During the U.S. Revolutionary War in 1776, problems with supply led to large-scale tobacco farming in Africa and Asia by the 1800s. The glut in world production that resulted led to a decline in prices, making the hitherto luxury product more affordable, and thus fueling even greater demand.

In the early twenty-first century, tobacco was the world's most widely cultivated non-food crop,

cultivated in about 120 countries of diverse climates. It is favored by farmers because of its performance under widely varying climatic and soil conditions. The largest producers of tobacco leaf as of 2008 were China, the United States, India, Brazil, Turkey, Malawi, and Zimbabwe.

TECHNOLOGICAL DEVELOPMENTS IN THE PRODUCTION OF TOBACCO PRODUCTS

As tobacco has become a valuable commercial crop, techniques for growing and curing the leaf developed in sophistication. Different varieties of leaf are grown, varying in the growing conditions needed, taste (due to level of dextrose), and burning properties. Among the most popular are Virginia, Burley, and various Oriental tobaccos, with most products blending different leaf varieties. Once harvested, tobacco leaf is subject to various methods of processing. The most important is curing, which enhances the flavor of tobacco and increases its preservation by reducing the moisture level of the leaf. Initially leaf was naturally cured in the sun or by air, but artificial methods using fires or flues were used for larger-scale production. In 1839 it was discovered that flue-curing turns leaf grown on infertile sandy soil a bright yellow and orange color, thus establishing the lucrative *brightleaf* industry. Over time, various fuels to cure tobacco came to be used, including coal, oil, gas, and wood. There has been an ongoing search for more cost-effective and energy-efficient uses of oil and gas, alongside improvements in barn and furnace design, to reduce fuel requirements. In the early 2000s, many countries bulk-cure their tobacco in barns constructed out of metal that guarantee better pane insulation, more precise atmospheric control, reduced labor requirements, and more efficient energy use.

There are many ways that tobacco can be consumed. Smokeless tobacco products can be sniffed through the nose (powdered snuff), chewed, or dipped (placed between the cheek and gum). In Europe, snuff remained the most popular way of consuming tobacco until the nineteenth century. Chewing tobacco was also popular; in the United States, it was associated with cowboys from the nineteenth century, and in many parts of Asia, as part of everyday social life for men and women.

Smoking tobacco has been the main method of consumption since the late nineteenth century. Pipes were first used by North American Indians for medicinal and ceremonial purposes, and clay pipes became fashionable in Europe from the sixteenth century among both men and women. In East Asia, pipes were made of bamboo and sometimes ivory, whereas throughout the Ottoman Empire, men smoked waterpipes (also known as narghile, hookah, and shisha). The discovery of *meerschaum* (a soft white mineral) in the eighteenth century led to the production of fine quality carved pipes. For common use, wooden pipes progressively replaced fragile clay pipes, with briar burl becoming the material of choice.

The first cigars (from the Mayan word for smoking) originated in Cuba, which still produces the most sought-after cigars. Imported to Europe and the United States in the eighteenth century, cigars became popular among the wealthier classes. By the nineteenth century, smoking rooms began to be introduced on trains, and in private clubs and hotels, and the smoking jacket became fashionable. During the twentieth century, cigarillos (mini cigars) became a fast growing segment of the tobacco market, especially among cigarette smokers seeking to reduce the amount smoked, and by cigar smokers wanting to reduce costs.

The most common way of consuming tobacco since the late nineteenth century has been the cigarette. While early forms of cigarettes are believed to date from Central America in the ninth century, the rolling or stuffing of paper-wrapped cylinders with cured and finely cut tobacco leaves is attributed to Ottoman Turks around the 1830s. In 1843 the French tobacco monopoly began to manufacture cigarettes. In 1847 Philip Morris opened a shop in London selling hand-rolled Turkish cigarettes, switching to making his own in 1854. Because the process of hand rolling was slow (four cigarettes per minute) and labor intensive, cigarettes remained relatively expensive. The invention of the cigarette rolling machine in 1880 by James Bonsack, which could produce 12,000 cigarettes an hour, opened the way for mass production and consumption. James Buchanan Duke, later the first chairman of British American Tobacco (BAT), licensed the machine and by the late 1880s, the Duke Company was producing four million cigarettes per day. Alongside increased production, manufacturers developed new blends of tobacco leaf and

other ingredients, which gave specific brands a distinct flavor. One key ingredient was reconstituted tobacco which, given additives to make nicotine more volatile when burned, also made cigarettes more addictive.

In 2007, cigarette companies worldwide produced around 5.5 trillion cigarettes, representing around 96 percent of the world tobacco market. The top five consuming countries are China (1,643 billion), United States (451 billion), Japan (328 billion), Russia (258 billion) and Indonesia (215 billion). While the global cigarette market continues to grow, awareness of the harmful health effects of smoking has led to efforts to develop products of varying effect that seek to reduce harm, including the introduction of filters, lowering tar levels, nicotine replacement therapy (NRT), and smokeless products.

OPPOSITION TO TOBACCO USE AND ITS CHANGING RATIONALE

Efforts to control tobacco use largely date from the seventeenth century and initially focused on immorality and economic protectionism. Catholic and other spiritual leaders denounced the increasingly popular practice, some banning it from religious venues. King James I published *A Counterblaste to Tobacco* in 1604, introduced a 4,000 percent tobacco import tax to stem debauchery, and made imports a royal monopoly in 1614. In 1612 the Chinese emperor Kangxi passed an edict forbidding the planting and use of tobacco. Prohibition was introduced in Japan around 1620, and in Russia under the Romanoffs between 1613 and 1689. In 1683 Massachusetts and Pennsylvania forbid the smoking of tobacco outdoors for fear of fire. Various penalties were introduced, ranging from excommunication to execution.

The rapid growth in tobacco's popularity, and the lucrative profits generated, led to the repeal of most restrictions until the early twentieth century. In many countries, governments sought to exert monopoly control over production and trade, while the medical professions even claimed tobacco offered health benefits. *The Lancet*, for instance, stated that smoking cigarettes in moderation could help sufferers of tuberculosis. There remained limited opposition to tobacco use until the late 1800s when antismoking organizations began to form in Europe and the United States to encourage moderate use among adults. These organizations failed to attract mass support until the early 1900s when attention switched to smoking among children as a detriment to their physical fitness and morality. Legislation prohibiting the sale of tobacco products to children was first adopted at this time.

Health-based concerns about tobacco began to influence broader regulation from the 1930s onward. Statisticians for insurance companies began to link smoking to cancer and reduced life expectancy. German scientists, as part of the Third Reich's so-called Gesundheitspflicht (duty to be healthy) campaign, were among the first to link tobacco to lung cancer. By the end of the Second World War, alarming increases in morbidity and mortality from lung cancer brought more scientific and medical evidence to the fore. The work of Argentinian Angel Honorio Roffo showed that cancer all along the "smoking highway" (lips, tongue, throat, cheek, bronchial passages) was caused by exposure to tars released in the course of smoking (Proctor, 2006, p. 494). In Britain, Richard Doll and Austin Bradford Hill published their seminal paper in 1950 linking smoking to carcinoma of the lung. Ernst Wynder and E. A. Graham reported similar findings in the United States the same year. Over the next ten years, rapidly accumulating evidence of harmful health effects led to the publication of *Smoking and Health* by the Royal College of Physicians in 1962, and the *Report of the U.S. Surgeon General* in 1964.

By the 1980s, accumulated medical and scientific evidence showed smoking to be a known or probable cause of around twenty-five diseases, including various cancers, heart disease, and emphysema. Policy measures aimed at reducing demand by tobacco users, such as higher taxation, health warnings, and education, were widely introduced in established markets such as the United States and Europe. The health risks to nonsmokers (notably children, spouses, and coworkers) from secondhand smoke prompted measures to ban smoking in public places from the early 1990s. Other measures to regulate tobacco use included restrictions on marketing, advertising, and promotion; product design; and ingredients disclosure.

Throughout the second half of the twentieth century, public health advocates decried the pace and strength of regulation, weakened by the economic importance and political influence of the

tobacco industry. The release of internal documents of the tobacco industry in the late 1990s revealed a well-organized and resourced campaign by the industry to undermine tobacco control efforts. The strategy included the funding of scientists to generate contrary evidence, lobbying of policy makers, and mobilizing of diverse allies to argue for the protection of civil liberties. The exposure of these tactics, along with data by the World Health Organization (WHO) attributing five million deaths annually to tobacco worldwide, led to growing support for stronger supply-side measures to control tobacco use. The adoption of the WHO Framework Convention on Tobacco Control (FCTC) in 2005 signalled recognition of the need for collective efforts across countries to strengthen both supply and demand side measures.

NEW SCIENTIFIC DEVELOPMENTS AND THE CONCEPT OF ADDICTION

In 1527 Archbishop Bartolomé de Las Casas Cuzco of Spain is believed to be the first to write about tobacco's adverse effect on the brain, notably the inability of American Indians to stop smoking. However, nicotine addiction or dependence is a relatively recent concept whose definition has evolved over time. Prior to the 1920s, addiction was seen largely as a type of excessiveness, attributable by some to moral vice. From the late 1920s, research sought to find psychological correlates with the withdrawal of narcotic drugs, such as morphine, after prolonged use. This approach remained popular into the early 2000s, with addiction conceptualized as an uncontrollable disease and applied to the use of other substances, notably alcohol. A popular view of addiction in the 1960s, based on an assumption of physiological dependence by the user, refers to a state in which an individual needs to continue to take a drug in order to stave off unpleasant or dangerous withdrawal effects. The main shortcoming of this approach is that this motive plays a relatively modest role in the apparently unreasonable continued use of a drug. While many addicts experience withdrawal discomfort, this is only one aspect of a wider problem. Indeed, individuals attempting to stop using drugs, including nicotine, continue to relapse at a high rate long after withdrawal symptoms have resolved and controlling such symptoms may be insufficient to prevent relapse. Another outmoded definition of addiction is inclusion of the concept of *intoxication*. This view holds that addictive drugs lead to changes in users' psychological state, leaving some degree of impairment.

Since the late 1980s, generic criteria for defining substance dependence, such as those developed by the American Psychiatric Association and the WHO, focused on difficulties in controlling the use of the drug, of giving priority to drug use over other important obligations, to continued use of the drug in the knowledge of harmful consequences, and tolerance to the effects of the drug. While the criteria apply generically to substance abuse, they are seen as a suitable framework for determining the addictive or dependent nature of nicotine and smoking. On the basis of these criteria, the UK Royal College of Physicians concludes that "nicotine delivered through tobacco smoke should be regarded as an addictive drug, and tobacco use as the means of nicotine self-administration" (2000, p. 85). Nicotine replacement therapies have come to be accepted as part of the support needed by tobacco users seeking to stop.

See also **Advertising and Tobacco Use; Britain: Tobacco Use and Policy.**

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KELLEY LEE

TOBACCO INDUSTRY

The tobacco industry is made up of the complex of primary suppliers, manufacturers, distributors

(both wholesale and retail), advertising agencies, and media outlets that produce, promote, and sell tobacco products. It also includes the law, public relations, and lobbying firms that work to protect these products from stringent public-health regulation and control.

The industry evolved in the late nineteenth and early twentieth century from many relatively small enterprises that produced tobacco products for puffing, snuffing, and chewing. The products of these small firms delivered nicotine to the nasal and oral mucosa. With the evolution and refinement of the cigarette, the industry developed first into a monopoly and then into an oligopoly in which a handful of major producers made a more sophisticated nicotine delivery system: a device that delivers nicotine by inhalation to the lungs and thence rapidly to the brain. Although its popularity is declining in the United States, cigarette use is increasing worldwide at over 2 percent per year, especially in much of Asia, Eastern Europe, and the former Soviet Union. An integrated system of suppliers, manufacturers, marketers, and sales outlets is constantly evolving to supply this vast and growing market. In the past, sophisticated legal and lobbying enterprises managed to protect this industry from the sort of regulation advocated by a number of public health groups—regulations that governments routinely impose on far less toxic products—but an admonition from an internal source as to the effects of tobacco led to a dramatic increase of public and regulatory pressure on the tobacco industry.

PRIVATE ENTERPRISE VERSUS STATE MONOPOLY

Tobacco (nicotiana) is a plant of the nightshade family (genus *Nicotiana*) and is native to the Americas; it was a major commodity of commerce in colonial times. Cigar tobaccos were key exports from the Spanish and Portuguese colonies of the Caribbean and South America, while tobaccos for snuff, pipe, and chew were the economic mainstays of the English colonies in Virginia, Maryland, and the Carolinas. Whereas most of Europe (and the rest of the world) established state-run monopolies for tobacco distribution, private enterprise was the vehicle of tobacco commerce in Great Britain (and eventually in the United States). The state monopolies provided both a popular product for the populace and revenue for the national treasury—but private enterprise, which always paid excise tax in Great Britain, was more resourceful in expanding the market. This phenomenon was exploited in the twentieth century and was especially apparent in the 1990s, with the remaining state monopolies becoming privatized and adopting the marketing techniques of the by-now enormous transnational tobacco companies, often actually merging with them.

FROM COTTAGE INDUSTRY TO MONOPOLY TO OLIGOPOLY

Relatively expensive, hand-rolled cigarettes became popular novelties in the United States and Europe in the mid-nineteenth century. The novelty came to dominate the industry over a period of forty years, from the mid-1880s to the mid-1920s, when, for the first time, more tobacco in the United States was used for cigarettes than for chewing tobacco.

A number of changes in the nineteenth century laid the groundwork for the cigarette's commercial success. The development of flue-cured tobacco and air-dried burley tobacco—easily processed into tobaccos for smoking (where the smoke might be inhaled) were major factors (Slade, 1993). Cigarette-making machines—first used commercially in 1883 by the American Tobacco Company—the development of safe matches, and an extensive railroad network to transport centrally manufactured cigarettes throughout the United States were among the other key factors responsible for this product's success.

Duke of Durham, North Carolina. These elements were successfully harnessed by Benjamin Newton (Buck) Duke, head of the American Tobacco Company. A working cigarette-making machine had been invented in 1881 by James Bonsack in response to a contest held by the cigarette maker Alan & Ginter of Richmond, Virginia (Smith, 1990). But the contest sponsors decided against using the invention since they did not know how to sell as many cigarettes as the machine was capable of making. Duke, however, realized that the low prices made possible by mass production, together with advertising to stimulate demand, would create a large enough market to absorb the vastly expanded production. He obtained favorable terms for using the machine in exchange for technical assistance in perfecting it. The machine Duke put on line in 1883

produced 120,000 cigarettes per day, the equivalent of 60 expert hand rollers. Duke's competitors had to pay more for Bonsack machines than he had, and Duke engaged in price wars to further weaken other manufacturers. Gradually, he bought out his competitors and monopolized the U.S. cigarette industry. By 1890, Duke controlled the cigarette market, and by 1910, just before his monopoly was broken, he controlled more than 80 percent of all tobacco products manufactured in the United States, except for cigars (Robert, 1952).

Seeking further growth, Duke began to expand his cigarette business overseas (Robert, 1952). By 1900, a third of the U.S. domestic production was being sent to Asia, and company factories were operating in Canada, Australia, Germany, and Japan. In 1901, Duke purchased a cigarette factory in Liverpool, England. Alarmed British manufacturers, seeking to avoid the fate of their U.S. compatriots, banded together as the Imperial Tobacco Company. The resulting trade war between American and Imperial ended in a truce. American was given exclusive trading rights in the United States and Cuba, and Great Britain became Imperial's exclusive territory. A new company, jointly controlled by both giants, was to sell cigarettes to the rest of the world. This modest sinecure was the birthright the parent companies gave the British-American Tobacco Company (BAT).

Antitrust Litigation. In 1907, the U.S. government filed an antitrust case against the American Tobacco Company. The result of this litigation was the dissolution of the trust four years later into a number of successor companies, some of which retain major roles in the U.S. cigarette market. These companies were the American Tobacco Company, the R. J. Reynolds Tobacco Company, Liggett & Myers, and P. Lorillard.

Once it had emerged from the confines of the trust, R. J. Reynolds, which had never before made cigarettes, developed and introduced Camel, a novel brand, in 1913 (Tilley, 1985). Camel was the first brand to combine air-dried burley, which had previously been important in chewing-tobacco products, with the then-conventional cigarette tobaccos—the flue-cured and Turkish (Oriental) varieties (Slade, 1993). Camel featured a coherent, national advertising campaign from N. W. Ayer that relied entirely on mass-media outlets in magazines and on billboards instead of on package-based promotions such as cigarette cards, coupons, and premiums. The legacy of this startling departure from the conventional cigarette-marketing techniques of the time is captured by the sly legend that still graces each pack of twenty unfiltered Camels sold in the United States: "Don't look for premiums or coupons, as the cost of the tobaccos blended in CAMEL Cigarettes prohibits the use of them."

The other factor that distinguished Camel from its competitors was its price. While the leading brands of the time, such as Fatima, sold for fifteen cents per pack of twenty, a pack of Camel sold for a dime. In short order, Camel overwhelmed the competition and ushered in a dramatic expansion of the domestic cigarette market. American Tobacco copied the Camel formula with Lucky Strike, and Liggett & Myers followed with its copycat product Chesterfield. Cigarette cards, premiums, and coupons were abandoned in favor of the mass media, and prices fell. Cigarette use, then only rising slowly, began an unprecedented increase. This growth continued virtually unabated for forty years or so, until it finally slowed and eventually reversed by alarms that lung cancer and other major diseases could be caused by cigarettes (Fiore et al., 1993).

Only two firms that had no roots in the tobacco trust have played major roles in the U.S. cigarette market (Sobel, 1978). After Buck Duke's death in 1929, BAT purchased the Brown & Williamson Tobacco Company in Louisville, Kentucky. BAT gradually built this company into a major cigarette producer. For decades, its Kool brand dominated the menthol category, and during the 1930s and 1940s, its Wings brand gained market share by undercutting the prices of the majors. Brown & Williamson continues to offer a full range of cigarettes for the U.S. market in the early 2000s. It also produces cigarettes for export to many of BAT's international markets.

The other upstart company was Philip Morris, which began its U.S. operations as a specialty cigarette maker in New York in the first quarter of the twentieth century. In addition to its standard brand called Philip Morris, it produced Marlboro—a cigarette for "ladies." The company expanded in the 1930s with a low-priced brand (Paul Jones) and a clever pricing scheme for Philip Morris English Blend (Robert, 1952; Sobel, 1978). It suggested

a retail price for the latter slightly above that for the major brands, but it gave retailers a larger margin, thus encouraging prominent display of the brand in stores. In the mid-1950s, Philip Morris gave Marlboro a filter and had the Leo Burnett advertising agency remake its image entirely to one of rugged masculine outdoor daring on horseback. (The entire sweep of Marlboro advertising is included in the special advertising collection of the American Museum of National History in Washington, D.C.) By the mid-1970s, Marlboro was the leading U.S. cigarette and by the 1990s, thanks to the strength of Marlboro's appeal to teens and young adults, Philip Morris overtook R. J. Reynolds to become the nation's largest tobacco-product manufacturer.

Smokeless Tobacco. Moist snuff and chewing tobacco enjoyed a 1980s and 1990s resurgence in popularity—this is based on the successful efforts of U.S. Tobacco (UST). It sells oral tobacco (e.g., Skoal Bandits, Skoal, Copenhagen) to adolescents and preadolescents (Denny, 1993). Oral tobacco is the only category of tobacco product whose consumption increased in the 1990s and early 2000s in the United States. This increase is attributable to UST's innovative marketing of moist snuff to adolescent boys and to imitation products from other manufacturers. Although UST envisions a global market for snuff, the World Health Organization has declared that countries in which oral tobacco is not a traditional product should ban it. A number of countries—including Australia, New Zealand, Hong Kong, and the European Community—have taken this step, often defying intense pressure from the U.S. government when doing so.

INNOVATION

The tobacco industry adapts to changing circumstances in many ways. Product innovation is a key strategy. Since the early 1950s, the major changes in cigarette design have come in response to public-health concerns that cigarettes constitute a leading cause of illness and death (McGinnis, 1993; Slade, 1993). Most of these innovations have been variations on filters and so-called low-tar designs. Ballyhooed with multibillion-dollar advertising budgets, these innovations propped up cigarette consumption over the years despite the complete absence of demonstrated benefit at the time they were introduced. Years of study (and as many years of unregulated sale) have only produced evidence for decidedly marginal benefits, yet the innovations have become firmly established. These supposed advances have been criticized by some as being nothing more than public relations gimmicks in the face of and in mocking response to profound public-health problems.

The cigarette companies continue in the early twenty-first century to invent novel ways to deliver nicotine to the brain. Electronic devices, smokes with charcoal fuel elements, and tiny aerosol cans are but some of the gimmicks the companies have patented to facilitate the inhalation of nicotine. Despite these efforts, the industry remains dependent on smoking, with variations of the tobacco-filled cigarette the mainstay of its business for the foreseeable future.

INTERNATIONAL EXPANSION

Cigarette smoking has been declining in the United States, Canada, and Western Europe. Since the 1960s, however, the biggest cigarette manufacturers (BAT, Philip Morris, RJR/Nabisco, and, later, Japan Tobacco Incorporated) have steadily increased their business in international markets (Taylor, 1984). This expansion has been accompanied by the weakening and dissolution of both national private and state-owned tobacco companies. The process got under way in Latin America in the 1960s, spread to eastern Asia in the late 1980s, and developed into a frenzy of deal making in Eastern Europe and the republics of the former Soviet Union in the early 1990s (Shepherd, 1985; Sesser, 1993).

Shepherd has described the process whereby a transnational corporation moves toward dominating a formerly self-contained market through product innovation, smuggling, aggressive advertising, and pricing policies. The result is a larger market for tobacco products than existed previously and a corporate management that is better able to oppose public-health efforts at regulation and control. Although cigarette consumption is down in the United States, Canada, and Western Europe, it is rapidly growing in most of the world—especially the so-called third world. The transnational companies have positioned themselves to both fuel and profit from this trend. In an effort to reduce the public health impact from global expansion, the

World Health Organization created the Framework Convention on Tobacco Control in 2007, giving support from wealthier nations to those in mid-low income nations to fight against tobacco company marketing efforts.

DIVERSIFICATION

The giant cigarette makers have invested their tobacco profits in other enterprises for more than twenty years, ranging from soft drinks and cookies to office products, insurance, and real estate. This process has resulted in the ownership by tobacco companies of some widely known consumer-product companies, including Kraft and Nabisco. Although the parent tobacco companies pretend that this phenomenon makes them somehow less involved in tobacco (none now has the word "tobacco" in its corporate name), a thoughtful examination of these businesses reveals the following:

- Tobacco products remain by far the most profitable sector of each of these conglomerates; and tobacco products are always responsible for most of the company profits.
- Not one of these companies has backed away from any available opportunity to sell tobacco products. Indeed, the strongest companies continue to invest in domestic and overseas ventures that have as their goal the expansion of tobacco consumption.
- These companies make ready use of nontobacco subsidiaries to support their tobacco businesses. For example, RJR/Nabisco fired the ad agency that did their Oreo Cookie advertising after that agency also produced ads promoting an airline offering smoke-free flights. Philip Morris has used one of its Kraft-General Foods warehouses for its coupon-redemption program for the Marlboro Adventure Team.

Tobacco companies do not diversify to get out of the tobacco business. They diversify because tobacco has given them profits, the acquisitions seem to be sound investments, and the resulting product mix complements the core business in some manner.

PRICE WARS

Price competition has long been part of the tobacco industry strategy. It was the major tool for the achievement of monopoly power in the 1880s and was a key element in the early twentieth-century dominance of the market by Camel. In the 1930s, price competition, made possible by overly aggressive price increases by the majors, contributed to the emergence and growth of Brown & Williamson and Philip Morris (Sobel, 1978). From the end of World War II (1945) until 1980, however, price competition was virtually absent from the U.S. cigarette market.

In 1980, tiny Liggett & Myers, a firm that had become too small to enjoy oligopolistic profits, broke ranks with its fellows by introducing generic cigarettes. The strategy was made possible by the pattern of price increases in the industry—increases that had exceeded the rate of inflation for years. Brown & Williamson soon followed suit with its own generic brands, and within a few years every cigarette manufacturer had a multitiered pricing structure, with the heavily advertised, standard brands at the top. Prices for the major brands continued to rise steeply, far faster than inflation, through early 1993. Customers who might have stopped smoking because of high prices were kept in the market by the increasingly available lower priced offerings. By early 1993, however, investment analysts had become concerned because lower priced brands accounted for more than 25 percent of all cigarette purchases—with attendant threats to profits—and Philip Morris had become alarmed by the market share losses sustained by its cash cow, Marlboro, to less than 25 percent of all cigarettes sold.

Philip Morris had a number of key strengths that gave it a flexibility not possessed by its competitors, including market leadership, an absence of corporate debt, and a strong youth market for Marlboro. Its principal competitor, RJR/Nabisco, had an enormous corporate debt—and although Camel had been making inroads into Marlboro's youth market, it was still far from the dominant cigarette. These factors led Philip Morris to cut prices substantially (while mounting the most elaborate promotional campaign ever seen in the industry). The competition was forced to follow suit with lower prices. Marlboro's brand share surged; the threat to profitability from lower priced brands subsided; and the competition was left somewhat weakened.

LOBBYING AND PUBLIC RELATIONS

In 1915, the U.S. tobacco industry formed the Tobacco Merchants Association (TMA) to lobby

against the anticigarette laws that had become a problem for the industry in a number of states (Robert, 1952). These laws came about as a result of the efforts of antitobacco advocates, including Henry Ford and Thomas Edison. The TMA accomplished its objectives: By 1930, the state prohibitions on cigarettes had been diminished to easily ignored prohibitions that only barred the sale of cigarettes to minors.

In the 1950s, the industry faced a more substantial challenge—proof that cigarettes caused lung cancer. In addition to putting cosmetic filters on the product and making outrageous claims for their benefit (P. Lorillard trumpeted its asbestos-filtered Kent as "the greatest health protection in cigarette history"), the industry developed a sophisticated public relations and lobbying capability (Wagner, 1971). The public relations firm of Hill & Knowlton organized the Tobacco Institute to meet the industry's public relations and lobbying needs. The cigarette makers also formed the Tobacco Industry Research Committee (later reorganized and renamed the Council for Tobacco Research) to create the pretense that the industry was conscientiously involved in biomedical research to get to the bottom of the smoking and health question (Freedman & Cohen, 1993).

Although speculation existed as to how diligently the tobacco industry would pursue smoking research, they did in fact do so, but their conclusions, giving more light to the fact that tobacco is addictive and harmful, were not released. Routinely called the *tobacco cover-up* it resurfaced in later years with much of its strength coming from Bennett S. LeBow's agreeing, in 1997, to put warnings on cigarette packs stating that smoking is addictive. Leaked internal documents also served as evidence of the dangers. In 1998, however, other tobacco companies still contested that tobacco was not an addictive drug. Discovery, through LeBow, of the industry's nondisclosure and the understanding that the industry had evidence of the threat of smoking, however, caused severe public attacks on the tobacco industry to be more common. Public campaigns have also been more potent with reducing youth smoking. Between 1998 and 2000 smoking had declined 54 percent in middle schools and 25.2 percent in high schools. Then, too, tobacco advertising legislation has weakened the strength of tobacco propaganda among youth populations by banning all advertising that is determined to be too appealing to a minor.

Company	Home office	Major brands
Cigarettes		
Phillip Morris (Altria)	Richmond, VA	Marlboro Basic Benson & Hedges Merit Virginia Slims
RJ Reynolds (Nabisco)	Winston-Salem, NC	Camel Kool Pall Mall Winston Salem Doral Natural American Spirit
Lorrillard (Loew's Corp)	Greensboro, NC	Kent Newport
Moist snuff		
UST	Stamford, CT	Copenhagen Skoal Bandits Skoal Classic

Table 1. Leading U.S. tobacco companies. Major tobacco-product manufacturers in the United States, the location of their corporate headquarters, and the major tobacco brands they market. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

As of 2008 more legislation was being proposed and being worked on to make nicotine a drug regulated by the FDA. Previously, the FDA has tried to apply regulations to tobacco and cigarettes as a nicotine delivery agent, but the courts had determined that Congress had not yet given the regulatory administration such authority, so new legislation must be passed for successful and lawful regulation. If such a bill is passed tighter control will be possible so that tobacco can be prohibited at public events where minors may be part of the targeted demographic, in response to public outcry. Furthermore, tobacco companies are prohibited from sponsoring public events and athletic competitions. In some states, legislation has also already been passed, and tried, winning large cash settlements to recover lost health costs suspected to be tobacco-use related. Included in some of these settlements have also been requirements for the tobacco companies to pay for more advertisements intended to reduce youth smoking. Despite the research, such as it was, the mounting costs to the tobacco companies because of law suits and penalties, and in the face of growing evidence of harm from a variety of other

quarters, the smoking epidemic continues into the early twenty-first century.

The Tobacco Institute, in alliance with the various branches of the industry, stood as a bulwark against public-health activities for a generation. After the Master Settlement Agreement in 1998, the Tobacco Institute was reduced to a Web site of searchable documents directly related to tobacco industry lawsuits. The Council for Tobacco Research has funded studies of marginal importance for public relations gain while operating a Special Projects branch for the benefit of tobacco-product liability defense. In these and other ways, the tobacco industry has attempted to insulate itself from significant regulation and from acceptance of any responsibility for the harm its products cause. Similar organizations exist to protect the interests of oral-tobacco manufacturers.

OWNERSHIP

The major tobacco-product manufacturers are publicly owned and traded corporations. As such, they are owned by their investors. Major institutions, including banks, insurance companies, and pension funds, hold the majority of shares in the tobacco industry.

The tobacco industry is a powerful oligopoly of product manufacturers in alliance with a network of suppliers and associated service organizations. Although its products form the leading cause of preventable death, it continues despite public sentiment and attempts to protect itself against appropriate regulation by extensive legal, public relations, and lobbying efforts. The industry is understandably driven by an interest in making money. It has never acted out of a primary concern for the health of its customers or the health of those around them. For a variety of reasons, including clever intervention by the industry, government has utterly failed to provide the sort of regulatory control expected when it comes to something as addicting and toxic as nicotine-containing tobacco products until a critical documentation leak occurred from within the companies of the tobacco industry.

See also **Advertising and Tobacco Use; Nicotine.**

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DEPENDENCE

As of 2006, there were about 45 million cigarette smokers in the United States, representing 21 percent of the adult population. Another 2 percent were cigar smokers, and 2 percent used smokeless tobacco (chewing tobacco or snuff) (*Morbidity and Mortality Weekly Report*, 2007). More than half of tobacco users are dependent on (addicted to) nicotine, an alkaloid that is the main psychoactive ingredient in tobacco. Most of them will have to try to quit several times before they are successful. Both the direct effects of nicotine on the body and behavioral associations with those effects learned over the years of tobacco use keep people smoking even when they want to quit.

The role of nicotine in tobacco use is complex. Nicotine acts on the body directly to produce effects such as pleasure, arousal, enhanced vigilance, relief of anxiety, reduced hunger, and body-weight reduction. Nicotine (whether in tobacco or nicotine-containing medications) can reverse the withdrawal symptoms that occur in a nicotine-dependent person trying to quit, when nicotine levels in the body fall. These symptoms include anxiety, irritability, difficulty concentrating, restlessness, hunger, depression, sleep disturbance, and craving for tobacco. Nicotine also acts indirectly, through a learning process that occurs when the direct effects of nicotine occur repeatedly in the presence of certain features of the environment. As a result of this learning process, called conditioning, formerly insignificant environmental factors become cues for the direct actions of nicotine. These factors can become pleasurable in themselves or they can serve as a triggering mechanism for lighting up a cigarette. For example, the taste, smell, and feel of tobacco often evoke a neutral response and sometimes repugnance in a nonsmoker. After years of experiencing the direct effects of nicotine in the presence of tobacco, however, a smoker finds the sensory aspects of tobacco pleasurable.

The indirect or conditioned effects of nicotine can be responsible for much more complicated learning than the learning associated with nicotine's direct effects. Conditioning is also the process whereby the situations in which people often smoke, such as after a meal, with a cup of coffee, with an alcoholic beverage, while doing a task at work, while talking on the telephone, or with friends who also smoke, become in themselves powerful cues for the urge to smoke. When people stop using tobacco, therefore, the direct effects of nicotine are not the only pleasures they must give up. They must also learn to forgo the indirect effects of nicotine: those experiences that, through learning, have become either pleasurable in themselves or a cue to smoke.

QUITTING

Many nicotine dependent smokers want to quit smoking; however, once dependence on nicotine or tobacco is established, cessation becomes difficult. The reasons for wanting to quit vary. The most common include (1) a concern for one's health, (2) a concern for the health of family members and others due to the harmful effects of secondhand smoke, (3) social pressure exemplified in laws by state or municipal governments prohibiting smoking in certain indoor locations (such as restaurants and bars) and outdoor environments (such as in areas within the vicinity of hospitals or schools); and (4) economic factors (cigarettes have become increasingly expensive).

Successful quitting of tobacco use usually occurs through a series of mental stages or steps (Prochaska & DiClemente, 1983): (1) *Precontemplation*: the smoker has no intention to stop smoking during this stage; (2) *Contemplation*: the person is thinking of quitting but not within the next six months; (3) *Action:* the smoker has a stop date and a plan that is or will be implemented within one month; (4) *Maintenance:* the person has discontinued the regular, daily use of tobacco for a minimum of one month. Most regular tobacco users go through these stages of change several

times before they are successful. Although developed in relation to smoking cessation, these stages of change have been applied to the process of stopping other addictive behaviors.

RELAPSE

Relapse is a cardinal feature of substance dependencies, including nicotine dependence. To paraphrase Mark Twain: Quitting smoking is easy, I've done it a thousand times. Most quit attempts that are successful in the short-term are followed by a return to smoking or other tobacco use within a few weeks, sometimes days, of stopping. For example, 66 percent of smokers who try to quit on their own or with minimal outside help relapse within two days, 90 percent relapse within three months, and 95 to 97 percent relapse within one year of quitting. The key to successful smoking cessation is an understanding of the particular triggers that provoke relapse and the strategies that are effective in preventing relapse. Withdrawal symptoms, which can begin within hours of the last use of tobacco, are important triggers for cravings to smoke again. Emotional reactions to stress, such as depression and anxiety, and environmental cues that have acquired an association with smoking can also serve as powerful triggers of urges to smoke.

MANAGING URGES TO SMOKE

To avoid succumbing to urges to smoke, former tobacco users must develop ways of coping with and managing triggers for smoking. Shortly after quitting, when the strength of withdrawal symptoms and environmental cues is greatest, behavioral techniques such as the following are helpful: (1) removing ashtrays from one's home and office, (2) leaving the table as soon as possible after meals and engaging in other activities such as talking, walking, or doing the dishes; (3) avoiding (at least temporarily) situations that used to occur with smoking, such as drinking alcohol, coffee, or other beverages linked with smoking; (4) avoiding situations in which other smokers are likely to be around, and (5) actively seeking social support for smoking cessation. The encouragement of a spouse, family members, or friends who are nonsmokers or who are in the process of quitting, can make it easier to avoiding lighting up again. Smokers who enjoy having something in their mouths or handling cigarettes can substitute something for these smoking-related tactile behaviors. They can chew gum, toothpicks, or sunflower seeds; munch low-calorie snacks; and snap, roll, or twist rubber bands on their wrist. What people think about while quitting is also an important factor for preventing relapse. Instead of thinking about the expected pleasures of a cigarette, the would-be quitter can substitute thoughts about the health hazards of smoking, the health benefits of not smoking, or the pleasures of an anticipated reward for not smoking.

These urges to smoke, or cravings, can re-occur long after the nicotine withdrawal period has ended, usually provoked by conditioned cues to smoking, frequently the onset of strong emotional events formerly managed by smoking. Applying the strategies learned during the weeks shortly after quitting can help the former smoker to overcome temptations to smoke that challenge one's ability to maintain abstinence in the long term.

INDEPENDENT QUITTING

Most efforts to quit occur without professional help. Persistence in avoiding a return to smoking is essential; most smokers try to quit several times before they are successful. Many aids are available to tobacco users who quit on their own. Smoking-cessation program guides and motivational and educational audiotapes and videotapes are obtainable from physicians, hospitals, or organizations such as the American Lung Association, the American Cancer Society, or the American Heart Association, or they may be found in bookstores and libraries.

ASSISTED QUITTING

Smoking-Cessation Programs. Resources for smokers who seek help for quitting are available in most communities in the United States. Smoking cessation clinics can be found in most hospitals and community health centers. Information regarding the location and availability of smoking cessation programs can be obtained from a nationally based telephone resource at 1-800-QUIT-NOW (1-800-784-8669).

Physician- and Clinic-Assisted Quitting. Physicians' offices and hospital clinics that offer

smoking cessation assistance are particularly useful for people who have medical problems, for people who have tried before and failed to quit, or for people who may benefit from smoking cessation medications. Smokers can turn to these health-care facilities for advice on how to quit, for self-help material, for support and information about other cessation resources that could be more suited to their needs, and if necessary, prescriptions for medications to ease the difficulties of withdrawal and increase their chance of successfully quitting.

Pharmacotherapies for Tobacco Dependence. Smokers who have tried to stop smoking on their own but failed are candidates for treatments with smoking cessation medications. First-line medications approved as cessation aids by the U.S. Food and Drug Administration (FDA) include the various nicotine replacement systems, such as nicotine chewing gum, nicotine patch, nicotine nasal spray, nicotine inhaler, and nicotine lozenge; and two non-nicotine medications, bupropion (Zyban) and varenicline (Chantix). Second-line medications, which are not FDA-approved for this indication, include nortriptyline and clonidine, and combination pharmacotherapy (United States Department of Health Human Services, 2008).

FIRST-LINE MEDICATIONS

The nicotine replacement therapies (NRT) when used as directed all approximately double the likelihood that a person will successfully quit smoking. NRT can reduce the severity of nicotine withdrawal. Research has suggested that prolonged use of these medications can extend the period of abstinence. Some tobacco users are concerned about the hazards of nicotine, but the hazards of NRT are much less than those associated with smoking. First, the amount of nicotine ingested through the replacement therapies is less than that taken in from cigarettes. Second, nicotine-replacement medications do not expose smokers to the other hazards of cigarette smoke, which include carbon monoxide, tar, cyanide, and a number of other toxic substances. On balance, using the nicotine replacement systems is much safer than smoking cigarettes. The nicotine-replacement medications are particularly useful with more seriously addicted smokers, but they are not a simple cure; rather, they should be used as part of a program of learning to live a tobacco-free lifestyle.

Nicotine Chewing Gum. The chewing gum is available without a prescription and comes in strengths of 2 and 4 milligrams (mg), although the dose actually delivered to the chewer is 1 mg and 2 mg, respectively. The 4-mg formulation has greater utility for heavier smokers (those smoking more than twenty cigarettes daily). Nicotine is absorbed from the gum gradually over twenty to thirty minutes, in the course of which blood nicotine levels are similar to those seen after smoking a cigarette. The gum should be chewed intermittently, to allow time for the nicotine in the saliva to be absorbed. Nicotine gum should be chewed regularly throughout the day, and when urges to smoke are felt. For maximum benefit, nicotine gum should not be chewed within ten minutes of drinking any beverage because certain beverages such as coffee, fruit juice, or cola drinks reduce the absorption of nicotine. Most people need to chew eight to ten pieces per day to obtain optimal benefits, usually for three to six months, but fewer pieces can be used during the later period of nicotine gum use. Side effects from chewing nicotine gum may include fatigue and soreness of the jaw, loosening of dental fillings, and occasionally nausea, indigestion, gas, or hiccups, particularly if one has chewed the gum so rapidly as to swallow nicotine-rich saliva.

Nicotine Patches. This formulation of nicotine treatment is also available as an over-the-counter medication. Patches deliver nicotine in its un-ionized (uncharged) chemical form, thereby allowing the drug to pass through the skin readily. Various patches deliver different doses and are applied to the skin once a day for periods that range from sixteen to twenty-four hours within the day. The higher dose patches (usually 21 mg) are used during the initial four weeks of quitting, and lower-dose patches (14 mg and 7 mg) are available for subsequent tapering. A single-dose nicotine patch (15 mg) used for sixteen hours during the day, which is recommended for eight weeks' use, is also available. Smokers who want to quit are instructed to first stop smoking and then to apply the patch daily, usually upon waking up. Side effects from nicotine patches may include itching or burning over the patch site, which usually subsides within an hour, and local redness and mild swelling. Some people experience a sense of stimulation, and occasionally, insomnia and vivid dreams. These effects tend to occur during the

first few days of patch use but diminish with longer patch use. There was initial concern regarding the cardiovascular safety of smoking while using the patch, though this has not been borne out. Nicotine patch users who are unable to resist one or two cigarettes are much better off keeping the patch on, to prevent a full-blown return to smoking, rather than removing the patch.

Nicotine Lozenge. The nicotine lozenge, like the nicotine gum, is an oral form of nicotine replacement and is also available as an over-the-counter medication. The nicotine lozenge comes in the form of hard candy, and should be dissolved in the mouth rather than chewed or swallowed. Patients are advised to use one lozenge every one to two hours, or a minimum of nine lozenges per day for the first six weeks, then to reduce to one lozenge every two to four hours during the seventh to the ninth week, and one lozenge every four to eight hours for weeks ten to twelve. Use beyond twelve weeks is not recommended. Patients should not drink or eat immediately before using the lozenge or while it is in the mouth. The most common side effects from nicotine lozenge are nausea, hiccups, heartburn, coughing, and headache. More nicotine is delivered through the lozenge than the gum because the lozenge dissolves completely whereas a residual amount of nicotine is retained in the gum. A comparison of safety profiles showed similar tolerability of the nicotine lozenge and the nicotine chewing gum.

Nicotine Inhaler. The nicotine inhaler consists of a plastic tubelike mouthpiece into which is placed a cartridge containing a nicotine-impregnated plug. Nicotine vapor is produced when warm inhaled air passes through the plug and nicotine is delivered through the buccal mucosa. The inhaler produces a rate of nicotine delivery similar to the nicotine gum. Eating and drinking acidic beverages such as coffee and juice should be avoided fifteen minutes before or after use of the inhaler. Dose is related to temperature; low temperatures will inhibit the release of nicotine. Use of the inhaler for up to six months with gradual reduction in frequency during the last two months is recommended. Clinical trials of the nicotine inhaler have shown that it doubles quit rates obtained with placebo, similar to the effects observed with the other nicotine replacement systems. Side effects from the inhaler include mild irritation of the mouth and throat, coughing, and runny nose. The frequency and severity of these symptoms decline with continued use of the inhaler.

Nicotine Nasal Spray. The nicotine nasal spray was designed as a more rapid means of delivering nicotine to the smoker than the gum or the patch. The nasal spray consists of a small bottle containing a 10-mg/ml nicotine solution. A 50-milliliter spray containing 0.5 mg nicotine can be conveniently delivered using an accompanying manual pump. Each dose consists of two squirts, one to each nostril. This mechanism can deliver nicotine to the brain within ten minutes, providing the most rapid nicotine delivery among the currently available nicotine replacement delivery systems. Patients are advised to use one or two doses per hour and may increase as needed. The minimum treatment is eight doses per day, with a maximum limit of forty doses per day or five doses per hour. The recommended duration of therapy is three to six months. The nicotine nasal spray has some potential to produce dependence manifested either in increased frequency of use or in longer duration of use than recommended, associated with its greater rapidity in producing nicotine effects compared to the other forms of NRT. The side effects associated with the nasal spray are irritation of the nose and throat, sneezing, coughing, and teary eyes. These symptoms often occur during the first week of use but typically decline with continued use.

Bupropion. Bupropion sustained release (SR) is a non-nicotine medication that is available by prescription only. Bupropion was originally marketed as an antidepressant (Wellbutrin). On the strength of evidence from several placebo-controlled trials, the FDA approved the marketing of bupropion (SR), under the trade name Zyban, as a treatment aid for smoking cessation. The mechanism by which bupropion assists smokers is not clear but it is thought to be related to both noradrenergic and dopaminergic activity in the brain. Patients are advised to begin using bupropion at a dosage of 150 mg per day for three days, then to increase to 150 mg twice a day for one to two weeks prior to a selected quit date, with continued treatment

for seven to twelve weeks following the quit date. Bupropion has been shown to reduce withdrawal symptoms and to reduce the weight gain usually associated with stopping smoking. The most common side effects reported by bupropion users have been insomnia and dry mouth. Bupropion is contraindicated in persons with a history of seizures, or of eating disorders, and those who have used a monoamine oxidase inhibitor in the past fourteen days. Recent research has suggested that extending bupropion use beyond eight to twelve weeks can increase the period of abstinence, although the risk of smoking again appears to return once the medication is no longer used (Covey et al., 2007).

Varenicline. Varenicline was approved by the FDA under the trade name Chantix as a treatment for nicotine dependence. The development of varenicline for smoking cessation was based on knowledge regarding the pharmacology of nicotine addiction, specifically the role of acetylcholine-receptor subtypes in the mediation of nicotine addiction. Through high affinity and high selectivity at the alpha4beta2 nicotinic acetylcholine receptor site, varenicline exerts agonist effects—reducing withdrawal symptoms, and antagonizing the effects of ingested nicotine—limiting the reward and pleasure associated with smoking. Industry-sponsored trials of varenicline, conducted among healthy smokers aged eighteen years or more who smoked at least ten cigarettes daily, showed that compared to placebo treatment, varenicline more than doubled the abstinence rate at the end of twelve weeks of treatment and at fifty-two weeks after the initial quit date (Lam & Patel, 2007). In addition, head-to-head trials showed higher abstinence rates at the end of twelve-week treatments and one year after quitting with varenicline compared to bupropion. A maintenance treatment trial showed that extending the treatment period by another twelve weeks modestly increased the abstinence rate, although the protective effect of varenicline seemed to abate upon discontinuing its use. The recommended dosing regimen is 0.5 mg once daily for the first three days, then 0.5 mg twice daily for days four to seven, and 1 mg twice daily to complete twelve weeks of treatment. Mild-to-moderate nausea was the most commonly reported side effect (about 30 percent of trial participants); other adverse events reported by more than 10 percent of study participants were headache, insomnia, and abnormal dreams.

Unlike bupropion, which had been available for several years as an antidepressant medication, the post-marketing information about the side effects of varenicline has been limited. Concerns have been raised regarding possible adverse reactions among smokers with comorbid psychiatric conditions, for example, schizophrenia and bipolar disorder, who were excluded in the pivotal clinical trials; further research to determine varenicline's safety and efficacy among such populations is needed.

SECOND-LINE MEDICATIONS

Clonidine (Catapres) is an alpha2-noradrenergic agonist that was initially used for the treatment of hypertension, and subsequently found to diminish symptoms of both opiate and alcohol withdrawal. The efficacy of clonidine as a short-term smoking cessation aid was demonstrated in several studies in which clonidine was delivered either orally or in patch form. This drug has not received FDA approval as a smoking cessation aid, however, and should be considered to be a second-line treatment to be used when first-line pharmacotherapies have not been successful. Clonidine use is associated with reductions in pulse rate and blood pressure, and abrupt discontinuation could result in a rapid rise in blood pressure and catecholamine levels. Side effects reported with clonidine use include dry mouth, drowsiness, dizziness, and sedation. Appropriate dosage levels have not been established as of 2008.

Nortriptyline is used primarily as an antidepressant (Pamelor). Results from several trials of nortriptyline as a smoking cessation aid have found that it can double the abstinence rate at the end of treatment, similar to the effect of bupropion. Nortriptyline has not been approved by the FDA for the treatment of tobacco dependence, mainly because of a more complicated side effect profile than the first-line medications (including cardiovascular changes), and the small number of trials that have evaluated nortriptyline for smoking cessation. In the smoking cessation trials, nortriptyline use was initiated at a dosage of 25 mg/day, and increased gradually to 75 to 100 mg per day over twelve weeks. Sedation, dry mouth, blurred vision,

urinary retention, lightheadedness, and shaky hands are the most commonly reported side effects of nortriptyline use.

Other Treatments. A number of other treatments have been used to aid in smoking cessation: hypnosis, acupuncture, lobeline and silver acetate medications. The effectiveness of these treatments has not been established by medical research, although some individuals may benefit from them. None of these treatments, however, can cure smokers of their tobacco addiction without the commitment and effort that are usually required to quit.

Combination Pharmacotherapies. Evidence from multiple published studies support the effectiveness of several types of combination treatments; these include nicotine patch + bupropion, nicotine patch + nicotine inhaler, long-term nicotine patch use (eighteen to twenty-four weeks) + ad libitum nicotine gum or nasal spray, nicotine patch + nortripyline, and nicotine patch + antidepressants (paroxetine and venlafaxine). All of these combination treatments significantly increased abstinence at the end of treatment and at twelve months follow-up. Individual patient characteristics, for example, depressed mood at the time of making the cessation attempt, and patient preference are useful indicators for selecting the appropriate type of combination treatment.

SMOKERS WITH PSYCHIATRIC CONDITIONS

There has been increasing recognition that tobacco use and nicotine dependence are more prevalent among individuals with psychiatric illness and substance use (alcohol or drugs) disorders. Persons with mental disorders comprise 20 percent of the population yet consume 44 percent of cigarettes and tobacco in the United States. The prevalence of nicotine dependence in the general population is about 13 percent but significantly higher among persons with mental illness or alcohol and substance use (other than nicotine) disorders (Grant et al., 2004). Several explanations for the high comorbidity of psychiatric illnesses and nicotine dependence have been considered: (1) because nicotine can affect brain structure, tobacco use, which typically starts during adolescence, can cause susceptibility to mental illness and drug dependence; (2) because nicotine exerts positive effects on mood as well as reduces psychiatric symptoms, nicotine could be used for self-medication; and, (3) common factors, such as genetics or shared environment, account for the susceptibility to nicotine dependence and mental illnesses. Empirical support for these mechanisms has been reported, making it possible that any single one of them or combinations thereof are applicable in individual cases where tobacco dependence and psychiatric conditions co-occur.

Although it is clear that there is a higher prevalence of tobacco use among mentally ill and drug dependent populations, the likelihood as well as the consequences of smoking cessation when psychiatric illness is present remain controversial. Epidemiological evidence has tended to show lower smoking cessation rates among persons with affective and anxiety disorders as well as persons with current alcohol and drug disorders, but contrary evidence has also been reported. Findings from clinical trials of smokers have also been mixed. It is possible that variation in severity or treatment of the comorbid disorder affects the likelihood of successful cessation. For example, a meta-analysis showed that among individuals who receive active treatments, for example, clonidine, bupropion, nortriptyline, or nicotine replacement therapy, or cognitive therapy for mood management, smokers stopped smoking at similar rates irrespective of whether they had a past history of major depression. However, among individuals who did not receive an active treatment (for example, those treated with placebo), a lower smoking cessation rate was observed among those with past major depression, particularly, the more severe, recurrent type of major depressive disorder (Covey, Bomback, & Yan, 2006).

Another clinically important but unresolved issue is the effect of smoking cessation on recurrence of mental illness or substance use relapse. Although more work remains to be done and exceptions have occurred, studies of persons with past major depression and schizophrenia have suggested that smoking cessation can occur without risk of exacerbating symptoms of the comorbid psychiatric condition (Hall, 2007). Studies of smokers with substance dependencies have also produced mixed results. A meta-analysis of nineteen trials of smokers who were either in treatment or recovering from substance dependence found

that smoking cessation treatment enhanced rather than impeded long-term sobriety (Prochaska, Delucchi, & Hall, 2004). Further studies of this important question are needed; however, a well-controlled trial of 499 persons receiving treatment for alcohol dependence showed that concurrent smoking cessation treatment resulted in higher rates of alcohol relapse compared to delayed smoking cessation treatment (Joseph et al., 2004).

Many persons who are dependent on tobacco want to quit but multiple barriers to tobacco cessation treatment remain. These include lack of knowledge about the availability of efficacious treatments, and lack of confidence on the part of smokers and health practitioners that tobacco cessation efforts will be successful. Removing these barriers are challenges to the public health and medical community. A significant barrier as well is the perception that cessation treatments are too expensive. In fact, tobacco cessation is one of the most cost-effective health interventions (Croghan et al., 1997) and, through its effect on reducing the morbidity and mortality of tobacco-related diseases, has the most far-ranging effects of any medical service in improving longevity and the overall quality of life (National Cancer Institute, 1997).

See also **Addiction: Concepts and Definitions; Nicotine; Nicotine Delivery Systems for Smoking Cessation; Treatment, Stages/Phases of: Relapse Prevention; Withdrawal: Nicotine (Tobacco).**

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MEDICAL COMPLICATIONS

The notion that smoking tobacco is injurious to the body is not recent. King James I of England, in his classic *Counterblaste to Tobacco*, written in 1604, outlined a number of beliefs about tobacco's ill effects on health and urged his subjects to avoid it. He called smoking a "filthie noveltie . . . A custome lothsome to the eye, hatefull to the nose, harmefull to the braine, dangerous to the Lungs." Opinions on the possible benefits and health damage caused by use of tobacco varied over the next three hundred years. Some nineteenth-century arguments that tobacco use injured health were linked to moral arguments against its use rather than to medical evidence (Corti, 1932).

In 1926, Sir Humphrey Rolleston of Cambridge University, who headed a committee on the use of

opioids, addressed the Harrogate Medical Society on the subject of medical aspects of tobacco and the possible toxic effects of nicotine (Rolleston, 1926). He drew few conclusions. Only a few health problems were clearly linked to tobacco: irritation of the throat and upper air passages by furfural, pyridine derivatives, ammonia, and carbon monoxide, which he ascribed to combustion of vegetable material and "not, like nicotine, in any way special to tobacco." Among the heart disorders Rolleston mentioned were extrasystoles (irregular heartbeats) and angina (pain caused by insufficient blood reaching the heart muscle). He noted that nicotine constricted the coronary arteries but suggested that people who suffered from extrasystoles might consider giving up coffee and tea before tobacco. He observed that cigarette smoking could cause arterial spasms and it was linked to obliterative diseases of the large arteries among young Jews living in London's East End. Rolleston believed that cancers of the lip and oral cavity observed in smokers were probably caused by syphilis and therefore not firmly linked to smoking. He devoted only a few lines to smoking's adverse effects on the respiratory tract, observing that smoking was responsible for "causing cough, hoarseness, bronchial catarrh, and so emphysema of the lungs." In general, Rolleston observed that considering "the large number of heavy smokers, the comparative rarity of undoubted lesions due to smoking is remarkable." He concluded that "to regard tobacco as a drug of addiction may be all very well in a humorous sense, but it is hardly accurate."

By the late nineteenth century, tobacco use was widespread, but people used very small amounts, mostly in the form of pipes, hand-rolled cigars, chew, and snuff; smoking was rare. The low level (by twenty-first century standards) of cigarette consumption changed dramatically at the beginning of the twentieth century with the invention of the cigarette rolling machine and the safety match. In addition to these technological innovations, the aggressive marketing campaign beginning in the late 1880s led to a dramatic increase in cigarette consumption. Before 1925, marketing was targeted exclusively at men; afterward, marketing was also targeted at women.

The turning point in the public's perception of the adverse consequences of tobacco smoking came with the publication of the Report of the Royal College of Physicians in England in 1962 and the Report of the Surgeon General in the United States in 1964. These two reports documented the experimental, epidemiological, and pathological evidence linking tobacco smoking to a variety of diseases, the most notable of which were chronic obstructive pulmonary disease (COPD), lung cancer, and illness and death from heart disease. Many more reports on the health consequences of smoking followed these two pivotal publications. Since 1969, the Office of Smoking and Health of the U.S. Public Health Service has coordinated the annual publication of a Surgeon General's Report on the health consequences of smoking, with several of the reports focusing on specific topics. In approaching such major reviews of specific health consequences of smoking, the Office of Smoking and Health assigns recognized experts to review and summarize all the existing scientific literature on the topic and then draw some conclusions from it. Some of the special topics that have been considered are the changing cigarette (the implications for health of low tar/nicotine cigarettes and filters) (1981), chronic obstructive lung disease (1984), cancer and chronic lung disease in the workplace (1985), nicotine addiction (1988), tobacco use among young people (1994), women and smoking (2001), and the health consequences of involuntary exposure to tobacco smoke (2006).

The 1979 and 1989 reports were overall reviews of the field, marking the fifteenth and twenty-fifth anniversaries of the landmark 1964 report produced when Dr. Luther Terry was Surgeon General. The 1979 report described tobacco smoking as "the largest preventable cause of death in America." In a 2004 report, tobacco smoking was expected to cause 170,000 cancer deaths; up to 200,000 deaths from cardiovascular disease; and more than 101,000 deaths from chronic pulmonary disease in 2008 (U.S. Department of Health and Human Services, 2004). As of 2008, cigarette smoking remained the most important cause of preventable disease and premature death in developed countries. It is estimated that, depending on the age at which a person starts to smoke, seven to thirteen years of life are lost to smoking-related diseases. Nonetheless, nearly forty-five million Americans continue to smoke and the economic costs of smoking are estimated at $167 billion annually (Centers for Disease Control and Prevention, 2007).

Other agencies, national (U.S. Environmental Protection Agency [EPA] and California Environmental Protection Agency [CalEPA]) and international (International Agency on Cancer Research [IARC]), have published comprehensive reports on tobacco and health. In particular, the CalEPA analyses tend to lead conclusions by the Surgeon General. For example, the CalEPA identified secondhand smoke (SHS) as a cause of heart disease in 1997; the Surgeon General did not do so until 2006. In 2005, the CalEPA concluded that SHS caused breast cancer in younger, primarily premenopausal women; in 2006 the Surgeon General concluded that the evidence is suggestive (one step below causal) (California Environmental Protection Agency, 2005, p. ES-4).

THE PHARMACOLOGICAL ACTIONS OF NICOTINE

Nicotine, the addictive component in tobacco, is responsible for the effects of tobacco use on the neural, cardiovascular, endocrine, and skeletal muscle systems. The most important effects are on the brain. It has stimulant (increased attentiveness, heart rate, and blood pressure) and mild depressant effects. Its effects are determined by the dose and rate of administration, hosts' tolerance, and rate of elimination. The addictive nature of nicotine is demonstrated by the return to smoking by those who have had serious smoking-related illnesses. Further, among those who quit, fewer than 10 percent are abstinent one year later (Benowitz, 2008). Pure nicotine is a poison that can kill within minutes by causing respiratory failure. Nicotine poisoning most commonly results from accidental ingestion of insecticides containing nicotine. A fatal dose of nicotine for an adult is forty to sixty milligrams.

Nicotine is quickly absorbed through the skin, mucous membranes, and lungs. Absorption through the lungs produces measurable effects on the central nervous system in as little as seven seconds. This rapid rate of absorption means that each puff on a cigarette produces some reinforcement of the smoking habit.

As early as 1963, scientists within Brown & Williamson and BAT Industries (formerly British American Tobacco) recognized that nicotine was addictive (Slade et al., 1995). In response to the public concerns about the health dangers of smoking, the tobacco industry has developed and marketed low tar and low nicotine cigarettes. Given nicotine's addictive nature, people smoke to maintain a target level of nicotine in their blood, and respond to low nicotine cigarettes by increasing their amount smoked or the number of puffs per cigarette, or by puffing more deeply or inhaling longer. Therefore, any possible benefits from switching to lower tar or nicotine cigarettes may be offset by this tendency of smokers to adjust their smoking behavior to maintain blood nicotine levels.

TOBACCO-RELATED DISEASES

Cancer. Tobacco smoking has been shown to be the major cause of lung cancer in both men and women. The increased risk for lung cancer depends on the number of cigarettes smoked per day, the degree of inhalation, and the age at which the adult began smoking. The risk of death from lung cancer is about twenty times greater for men who smoke two packs a day than for those who have never smoked. It is about ten times higher for those who smoke one-half to one pack a day. Mentholated and low tar cigarettes have also been shown to increase the risk of lung cancer. Tobacco smoking is synergistic (produces a multiplier effect) with the effects of other carcinogenic risks, such as exposure to radon or asbestos. Smoking is also synergistic with alcohol in causing cancers of the oral cavity, larynx, pharynx, and esophagus. In addition, smoking has been found to increase the risk of breast cancer, particularly in young premenopausal women and those who start smoking in their teen years when the breast is still developing.

Cardiovascular Disease. Smoking is the major cause of coronary heart disease (CHD); risk of death from CHD is 70 percent higher for men who smoke, with a similar effect for women. The risk of CHD from smoking is mediated through increases in blood pressure, oxygen demand, heart rate, and oxidative stress. In addition, it decreases the blood's oxygen carrying capacity and the ability of muscle to convert oxygen into energy. Smoking increases the risk for stroke. For example, women who smoke twenty-five cigarettes or more per day have a risk for stroke almost four times higher than nonsmokers. Smoking also increases the risk of atherosclerosis (formation of plaques) in the

peripheral arteries and the aorta. In addition, it leads to arterial endothelial dysfunction. The endothelium, which is the arterial layer that comes into direct contact with blood, is vital for arterial dilation and contraction, and prevents cholesterol from sticking to the arterial wall.

Lung Disease. Chronic obstructive pulmonary disease (COPD) includes three related disorders: chronic mucous hypersecretion that causes cough and phlegm production; airway thickening and obstruction of expiratory airflow; and emphysema—abnormal dilation of alveoli (air sacs responsible for gas exchange) and destruction of their walls. Cigarette smoking is the major cause of COPD. Compared to nonsmokers, male smokers are three times more likely and female smokers are twice as likely to have a persistent cough.

Other Medical Disorders. Other medical disorders include peptic ulcers, upper respiratory infections, osteoporosis, erectile dysfunction, dental and eye diseases, and cancers of the pancreas, bladder, and esophagus.

Conclusions Regarding Causality. Over time, the strength of the evidence linking tobacco with disease has mounted, new conclusions have been added, and older conclusions strengthened. To summarize conclusions regarding causality, both the Surgeon General and the CalEPA have followed the classification used by the Institute of Medicine and IARC. In this classification, a four-level hierarchy is established based on the available evidence (U.S. Department of Health and Human Services, 2004, pp. 17–29).

Category A. Evidence is sufficient to infer a causal relationship: Cancers of the lung, larynx, pharynx (oral cavity), esophagus, pancreas, bladder and kidney, cervix, stomach, and acute myeloid leukemia. Coronary heart disease (including heart attacks), stroke, and aortic aneurysms are also under this category. In addition, acute respiratory illnesses (including pneumonia) and chronic obstructive pulmonary disease are included. Breast cancer, as evidenced by research published after the year 2000, has also been found to be increased by smoking (Johnson, 2005).

Category B. Evidence is suggestive of a causal relationship: Cancers of the colon and liver, and erectile dysfunction.

Category C. Evidence is inadequate to infer the presence or absence of a causal relationship: Ovarian cancer, asthma onset in adulthood, and congenital malformations in general.

Category D. Evidence is suggestive of no causal relationship: Prostate cancer.

The effects of tobacco use are not limited to specific diseases that lead to death. Tobacco use can stimulate enzymes in the liver, which can result in alterations in the way various medications are metabolized. This alteration in metabolism can mean that the levels of medications in the body will not be high enough to be optimally therapeutic.

The risk for most diseases can be decreased by smoking cessation, but not all risks decline at the same rate. Cardiovascular disease risk falls halfway back to that of a never-smoker in just one year, and is almost (but not entirely) gone within three to five years. The risk of cancer declines more slowly, with some elevated risk still evident ten years after cessation. Within five years of quitting, overall risk of premature death drops by 50 percent (Shopland & Burns, 1993).

Pipe and cigar smokers are also at an increased risk of premature death, with approximately the same relative risk as cigarette smokers of getting laryngeal and esophageal cancers. The mortality risk for users of smokeless tobacco (oral snuff and chewing tobacco) comes primarily from cancers of the oral cavity and throat (U.S. Department of Health and Human Services, 2004).

Psychiatric Disorders. Dependence on tobacco is associated with dysthymic disorder and other forms of depression. As of 2008, it is not known, however, whether depression prompts people to begin smoking or whether it develops in the course of dependence on tobacco. Mood disorders increase significantly during withdrawal from nicotine, and are common reasons for relapse.

WOMEN AND SMOKING

Women who smoke tobacco have the same risks for adverse effects as men. In 2007, deaths due to lung cancer among women exceeded deaths from breast cancer, becoming the leading cause of cancer death

for women. Some women are at special risk. Women who smoke and use oral contraceptives have an increased risk of cardiovascular disease, as well as cerebrovascular disease, including subarachnoid hemorrhage (bleeding between the brain and its protective covering inside the skull). In addition, women who start smoking early in their teen years also have an increased risk of breast cancer compared to nonsmoking women (California Environmental Protection Agency, 2005, p. ES-4).

Women who smoke have higher infertility rates than those who do not and are also more likely to have menstrual irregularities. They also have higher rates of ectopic pregnancy (abnormal implantation of the fertilized ovum outside of the uterus). Nicotine crosses the placenta, and because it constricts blood vessels, a decreased amount of oxygen is delivered to the fetus. In addition, smoking elevates the amount of carbon monoxide in the mother's blood so that it carries less oxygen to the fetus. Women who smoke during pregnancy have higher rates of premature detachment of the placenta (*abruptio placentae*), premature rupture of membranes, and preterm delivery. The greater the amount of tobacco smoked during the pregnancy, the higher the frequency of spontaneous abortion and fetal death and the greater the likelihood of delivering an infant that is smaller than normal. In the United States, smoking has been associated with a 20 percent increase in preterm births among women who smoked a pack a day or more compared with those who did not smoke. Women who stop smoking early in pregnancy increase their likelihood of having normal deliveries and normal birth weight babies (U.S. Department of Health and Human Services, 2001).

SECONDHAND SMOKE

Secondhand smoke, also known as environmental tobacco smoke, is the smoke breathed by nonsmokers and is a mixture of mainstream (inhaled by the smoker) and sidestream (emitted from the tip of the cigarette) smoke. SHS accounts for approximately fifty thousand deaths annually, including three thousand deaths from lung cancer and forty-six thousand deaths from heart disease (U.S. Department of Health and Human Services, 2006). It has been established as a cause of heart disease, lung and sinus cancer, respiratory problems in children (bronchitis and pneumonia, middle ear infections) and adults (asthma induction), and low birth weight and sudden infant death syndrome in newborns. Passive smoke exposure during pregnancy (e.g., living with a smoker) can adversely affect the birth weight of the baby. In addition, SHS is a cause of breast cancer in young, primarily premenopausal, women (California Environmental Protection Agency, 2005, p. ES-4). The cardiovascular system is particularly sensitive to the harmful effects of SHS (just thirty minutes of exposure is enough to harm the exposed individual's arteries) (Barnoya & Glantz, 2005).

Exposure to SHS during pregnancy is associated with a decrease in birth weight of twenty to one hundred grams. Infants born to mothers who smoke are far more likely to die before their first birthday, primarily as a result of respiratory complications and sudden infant death syndrome. Children of mothers who smoke seem in general more likely to suffer from colds, asthma, bronchitis, pneumonia, and other respiratory problems (California Environmental Protection Agency, 2005).

Tobacco control programs (tax increases, banning smoking in the workplace and advertising, smoking cessation programs, and other strategies) have led to a reduction in the prevalence of smoking in the United States. Banning smoking in the workplace has proven to be one of the most effective tobacco control strategies, as it decreases smoking prevalence, the number of cigarettes smoked by continuing smokers, and exposure to SHS (Fichtenberg, 2002). In addition, heart disease and lung cancer mortality decrease after the implementation of smoke-free environments (Fichtenberg, 2002; Barnoya & Glantz, 2004). To halt the spread of smoke-free legislation in the United States and worldwide, the tobacco industry has implemented several strategies, including hiring scientists to redirect public attention from SHS toward other sources of air pollution, lobbying politicians, and creating useless smoking and nonsmoking sections in public places.

In general, white males in higher socioeconomic groups have lowered their smoking rate more than women and members of ethnic and racial minorities and lower socioeconomic groups. Adult smoking prevalence in the United States

remained unchanged during the early 1990s but decreased from 1997 (24.7%) to 2004 (20.8%). Smoking prevalence by ethnic group is highest among American Indians/Alaska Natives (32%), followed by African Americans (23%), Whites (22%), Hispanics (15%), and Asians (10%) (Centers for Disease Control and Prevention, 2007). An estimated 20 percent of high school students (ninth to twelfth grades) were current smokers in 2005 (Centers for Disease Control and Prevention, 2006).

In contrast to the general decline in the prevalence of smoking in developed nations, the prevalence of smoking is increasing in developing and newly industrialized countries. By the year 2030, cigarettes will kill ten million people per year; 70 percent of this total will be in low- and middle-income countries (Jha & Chaloupka, 1999). In most of these countries, the tobacco industry has been successful in preventing the implementation of sound tobacco control measures.

See also **Advertising and Tobacco Use; Complications; Nicotine; Treatment, Behavioral Approaches to; Treatment, Pharmacological Approaches to; Treatment, Specialty Approaches to.**

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SMOKELESS

Tobacco has been used in various nonsmoked forms throughout its long history. Indeed, before the introduction of the mass-produced cigarette in the early twentieth century, smokeless tobacco,

including chewing tobacco and snuff, was the predominant form of tobacco use, and in some regions of the world, such as India, it remains so in the early twenty-first century.

The earliest uses of tobacco, dating back thousands of years, were probably through chewing the leaves of the plant or inhaling powdered tobacco through the nose (snuffing). Tobacco was held to have many uses among Native Americans, including as a medicine, wound healer, appetite suppressant, psychoactive agent, and as an aid to religious rituals.

Early Spanish explorers recorded their observations of the practice of chewing and snuffing tobacco among the natives as well as smoking. When tobacco was brought back to Europe it was used both in smoked form (cigars and pipes) and in smokeless forms. However, during the eighteenth and early nineteenth centuries, tobacco use in European society was most commonly in the form of snuff. The practice of snuffing became fashionable among the French aristocracy at the time. The offering and taking of snuff in social settings became highly stylized, and elaborate snuff boxes served to display one's refinement, rank and wealth. Snuff use subsequently gained broader popularity in other European countries, including England, and outside the elite circles.

In late nineteenth century America, chewing tobacco was widespread and at its peak of popularity. Spittoons became a fixture in many public places, such as public buildings and trains. In the early twentieth century, however, use of chewing tobacco declined as machine-rolled cigarettes, which were seen as more convenient and hygienic, gained popularity. Around 1900, 52 percent of all tobacco used in the United States was smokeless, but by 1952 that number had dropped to 6 percent (Lewis et al., 1999).

USE OF SMOKELESS TOBACCO PRODUCTS

The term *smokeless tobacco* refers to an extremely diverse range of products, including mass-produced manufactured products as well as traditional and handmade products. While smokeless tobacco products by definition contain tobacco as the principal ingredient, the tobacco may also be mixed with other ingredients. For example, the primary ingredients in *gutka*, which is widely used in the Indian subcontinent, include betel leaf, areca nut, and a variety of spices and flavors in addition to tobacco. Even within the United States, a wide range of different types of smokeless tobacco products with different characteristics are used, including chewing tobacco, dry and moist snuff, traditional oral tobacco products, such as *iqmik*, and novel products, such as tobacco lozenges. The popularity of different product types has evolved over time. For example, use of moist snuff or dip increased substantially toward the end of the twentieth century, making up over half of the smokeless tobacco market, whereas sales of chewing tobacco and dry snuff fell (Maxwell, 2004).

Overall sales in pounds of smokeless tobacco products in the United States have remained relatively unchanged, or saw only a slight decline, between 1988 and 2008. However, revenues and advertising and promotional expenditures increased steadily over the same period. In 2005, the five largest tobacco manufacturers spent $250.76 million on smokeless tobacco advertising and promotion; over 40 percent of that was spent on price discounts paid to retailers and wholesalers to reduce the price to consumers for smokeless tobacco products (Federal Trade Commission, 2007, pp. 3, 5).

According to the 2006 National Survey on Drug Use and Health, there are approximately 8.2 million people aged 12 or older in the United States who use smokeless tobacco. The prevalence of smokeless tobacco use in the U.S. population overall is substantially lower (3.3%) than that for cigarette smoking (25%). However, there are substantial disparities in smokeless tobacco use among subgroups of the population. While 6.6 percent of American males report current smokeless use, only 0.3 percent of American females report the same. Smokeless tobacco use is also substantially higher among whites (4.2%) and American Indian/Alaska Natives (6.5%) than among African Americans (1.7%), Asians (1.2%), and Hispanics (0.9%). Smokeless tobacco use is greater in rural areas; the proportion of smokeless tobacco use ranges from 10 percent in rural counties to only 2 percent in large metropolitan counties (Substance Abuse and Mental Health Services Administration, 2007). High prevalence of smokeless tobacco use has also been found among U.S. military personnel (24% reported use; Chisick et al., 1998) and among some athletes, particularly major league baseball players (36% reported use; Severson et al., 2005).

Use of smokeless tobacco among youth warrants particular attention both because its prevalence is higher and because it may serve as a pathway to nicotine addiction and use of other tobacco products. A national survey found that 12.6 percent of twelfth grade boys reported having used smokeless tobacco in the past 30 days, and prevalence was even higher among white boys in southern states (Nelson et al., 2006, p. 900). Moreover, some smokeless tobacco products may be more accessible to new users and more likely to appeal to adolescents. During the 1970s, smokeless tobacco use increased substantially among teens and young adults when new products were introduced that were more accessible to new users, with lower nicotine content and attractive flavorings (Connolly, 1995). And evidence suggests that users who begin with starter products, that are low in nicotine, are more likely to graduate subsequently to products with higher nicotine content (Tomar et al., 1995).

A number of studies suggest that adolescents who use smokeless tobacco may be more likely to progress to cigarette smoking, although the evidence is not consistent (Tomar, 2003; O'Connor et al., 2005; Haddock et al., 2001). Smokeless tobacco also poses a global public health challenge. In many regions of the world, such as in India, smokeless tobacco use is the predominant form of tobacco use. In the Indian National Family Health Survey, 20 percent (28.1% of men and 12.0% of women) of respondents reported chewing tobacco and/or *pan masala*, though these figures varied widely by region (Rani et al., 2003, p. 3). Also, data from the Global Youth Tobacco Survey show that students aged 13 to 15 surveyed in 132 countries were more likely to report using non-cigarette tobacco products (11.2%) than to report smoking cigarettes (8.9%; MMWR, 2006).

HEALTH EFFECTS

One International Agency for Research on Cancer (IARC) monograph on smokeless tobacco reported that there is sufficient evidence, based on epidemiologic and laboratory studies, to conclude that smokeless tobacco causes oral cancer and pancreatic cancer in humans (Cogliano et al., 2004). At least 28 different carcinogens have been identified in smokeless tobacco products (National Cancer Institute, 1992, p. 115). Additionally, measurements of carcinogen by-products in humans show that smokeless tobacco users are exposed to levels of tobacco-specific nitrosamines, among the most important tobacco carcinogens, that are as high or higher than cigarette smokers (Kresty et al., 1996). There is also limited but inconsistent evidence suggesting that smokeless tobacco use may be associated with cardiovascular disease (Gupta et al., 2004). And smokeless tobacco use is associated with other health outcomes, including oral mucosal lesions, leukoplakia, and periodontal disease.

However, assessing the health risks of smokeless tobacco products is complicated given the diversity of traditional and manufactured products in use and their different characteristics. One study of eleven smokeless tobacco product brands available in the United Kingdom found that levels of tobacco-specific nitrosamines varied 130-fold across the products and nicotine content ranged from 0.1 mg/g to 63.2 mg/g (McNeill et al., 2006). Additionally, moist snuff sold in Sweden has relatively low levels of nitrosamines compared with some other smokeless tobacco products, such as American chewing tobacco (Hoffman et al., 1995) or *toombak*, a moist snuff product found in Sudan (Idris et al., 1991). Moreover, the health risks experienced by any tobacco user vary depending not only on the type of product used but on how it is used, when the person started and/or quit, and concurrent use of other harmful substances.

ADDICTION AND TREATMENT

Smokeless tobacco products contain nicotine as a major constituent and users of smokeless tobacco products demonstrate signs of dependence similar to those in cigarette smokers, including tolerance with repeated use and symptoms of withdrawal upon cessation of use. Moreover, individuals who are dual users (those who use both cigarettes and smokeless tobacco) tend to have higher nicotine exposure levels and find cessation even more difficult to achieve than those who use only one type of product (Wetter et al., 2002).

However, the most promising strategies for helping smokeless tobacco users to quit are different than those for cigarette smoking. While drug interventions, including nicotine replacement therapy (such as nicotine patch or gum) and bupropion, have been shown to be effective in helping cigarette smokers to quit, studies in smokeless

tobacco users have not found a similar benefit (Ebbert et al., 2004). These treatments may help reduce unwanted side effects associated with nicotine withdrawal, such as feelings of craving or weight gain, but they have not been shown to have any impact on successful quitting over the long term (Dale et al., 2007). Yet there is strong evidence that behavioral counseling interventions are effective for helping smokeless tobacco users to quit. In particular, counseling patients in dental offices, where the effects of smokeless tobacco use on the mouth can be detected and explained, has been shown to increase success in quitting. Interestingly, similar interventions have not been found to be effective for cigarette smokers (Carr & Ebbert, 2006). Telephone counseling may also be useful in assisting smokeless tobacco users to quit, although larger studies are needed to support more specific recommendations. In general, the evidence regarding cessation in smokeless tobacco users is very limited compared to that for cigarette smoking.

HARM REDUCTION

While smokeless tobacco use causes cancer and other diseases, it is associated with a lower overall risk profile compared with cigarette smoking. Indeed, according to some estimates, the magnitude of this difference is vast (i.e., "consumption of non-combustible tobacco is of the order of 10-1,000 times less hazardous than smoking" according to Royal College of Physicians, 2002, p. 5). This difference has led some scientists to suggest that smokeless tobacco has promise as a *harm reduction* intervention for cigarette smokers. That is, smokers who have trouble quitting might reduce their risk by switching to a smokeless tobacco product in place of cigarettes. However, there is not sufficient evidence as of 2008 to demonstrate that this strategy is effective in practice. In other words, even if the product is less toxic, it is not clear whether smokers will successfully switch without relapsing or continuing to smoke. Critics of this approach have also suggested that promoting the use of smokeless tobacco as less harmful might lead to an increase in initiation of smokeless tobacco use by adolescents and other new users or have a negative impact on tobacco use cessation efforts (Hatsukami et al., 2004).

The Swedish Experience is often referred to as a sort of natural experiment in the use of smokeless tobacco for harm reduction (Foulds et al., 2003). Sweden has the lowest male smoking prevalence of any country in Europe (14% of adult men are daily smokers) and the lowest levels of tobacco related mortality (about half that of the EU overall). However, a significant portion of men (22%) report using oral smokeless tobacco, typically in the form of *snus*, a moist oral tobacco product. Some scientists have suggested that the low smoking prevalence (and lower mortality) is due to the use of snus in place of cigarettes. However, this trend may also be a result of broader social and policy influences. For example, in the early 1960s Sweden was one of the first countries to fund an organized tobacco control effort, including the development of cessation clinics and antismoking education programs (Mitchell & Wellings, 1998). Changes in popular culture also likely had an impact on behavior and national smoking trends, as popular portrayals of smoking shifted from accepting to negative (Torell, 2002).

EVOLVING MARKETPLACE AND POLICIES

In the late 1990s and early twenty-first century, a range of new smokeless tobacco products were introduced and marketed that may be more likely to appeal to new users, including youth. Some new smokeless products use attractive flavorings, such as mint or fruit flavors, and new delivery methods, such as lozenges or small pouches that eliminate the need to spit. Major cigarette manufacturers Philip Morris and R. J. Reynolds have also introduced new smokeless tobacco products using the familiar brand names Marlboro and Camel. Moreover, some smokeless tobacco manufacturers have introduced new marketing strategies, such as marketing smokeless tobacco products to smokers for situations in which they cannot smoke, given the increase in smoking restrictions in workplaces and public spaces (O'Hegarty et al., 2007). It remains to be seen as of 2008 whether these new strategies will lead to increased use of smokeless tobacco.

Policies and regulations around smokeless tobacco products vary widely across countries. Additionally, the policies and regulations applying to smokeless tobacco products are in many cases different than those for cigarettes. For example, in the United States smokeless tobacco product packages carry a different set of mandated health warnings than cigarette packages. Additionally, smokeless tobacco

products are taxed differently than cigarettes; in general they are taxed at a lower level and states use different formulas for calculating the taxes. Since 2001, the European Union has prohibited marketing of snuff products (but not cigarettes or chewing tobacco) in all affected countries except Sweden and Norway. However, the World Health Organization Framework Convention on Tobacco Control, the first global public health treaty, broadly applies to all tobacco products, including traditional and manufactured forms of smokeless tobacco.

See also **Advertising and Tobacco Use; Withdrawal: Nicotine (Tobacco).**

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MARK PARASCANDOLA

SMOKING CESSATION AND WEIGHT GAIN

Successful smoking cessation is associated with modest weight gain. The amount of weight gain tends to average 10 to 13 pounds in the first year after quitting, with most of this occurring within the first six months of abstinence. Individual characteristics influencing the amount of weight gain include gender and initial body weight, length and frequency of smoking behaviors, and other lifestyle factors such as type of diet and physical activity. The exact mechanism through which cigarette smoking affects energy expenditure and body weight is not fully understood and is likely a combination of several factors:

- There is a slight metabolic advantage to cigarette smoking, meaning that smoking increases heart rate and the overall level of energy that the body uses to function. Following cessation, basal metabolic level slows, which promotes weight gain.
- Smoking suppresses appetite and food intake. Animal research has shown that mice administered nicotine initially eat less than control mice but that meal size eventually increases. Similarly, some dieters attempt to use the appetite-suppressing effects of smoking to resist urges to eat and to help them eat less. However, over the long term smokers do not tend to eat less than nonsmokers.
- Following smoking cessation, food smells and tastes better and is, therefore, more desirable. In general, smoking serves as an appetite suppressant and during withdrawal from nicotine, appetite increases. Laboratory experiments have shown that during smoking withdrawal, people are likely to manage cigarette cravings with food and to report more enjoyment in the experience of eating. Among current smokers, short-term abstinence from smoking is associated with heightened cravings for cigarettes and food, as well as increased calorie and fat intake.

Through a combination of these factors, smoking suppresses body weight, and following cessation weight reverts to a higher natural set point. On the population level, smokers tend to weigh less than former-smokers, who in turn weigh less than never-smokers. It should be noted that although there are certain health benefits to lower weight, these benefits are greatly offset by the negative health impact of smoking.

SMOKING FOR WEIGHT CONTROL

For some smokers, concerns about weight may motivate the decision to begin smoking. Initiation of smoking by adolescent girls has been linked to weight concerns, and among young adults smoking is more common among those who are trying to lose weight. The cigarette industry appears to

capitalize on the weight concerns of its target market by producing advertisements that equate smoking with being slim. There is some evidence to suggest that smokers who are especially concerned about their weight have magnified beliefs in the ability of smoking to suppress weight; that is, they believe smoking to be much more effective at controlling weight than it actually is. Consequently, smokers who are especially weight concerned are less likely to report a desire to quit.

Weight concerns are also associated with unsuccessful attempts to quit smoking. One of the commonly reported reasons for smoking relapse is weight gain. Although concerns about weight gain are more common for female smokers than male, a significant portion of male smokers also report fear of cessation-associated weight gain.

TREATMENTS GEARED TOWARD WEIGHT CONCERNS

Smoking cessation treatments that include a component to address weight gain may be more successful for some individuals, especially those with heightened concerns about weight gain. Several treatment options have shown some promise, whereas others have been less successful.

Behavioral treatments for weight control may be effective for weight-concerned smokers. Examples of behavioral weight control treatments include moderate calorie-reducing diets and programs to promote physical activity. These treatments are most successful when administered as a supplement to standard smoking-cessation treatment and when promoting behavioral changes intended to result in very modest weight change. The DHHS 2000 *Clinical Practice Guideline* for treating tobacco use and dependence recommends that patients not attempt weight control until after they are confident that they will not resume smoking. Patients should be advised that strict dieting during a quit attempt could hinder successful cessation.

Cognitive Behavioral Therapy. Cognitive behavioral therapy (CBT) and other treatments to address body image and weight concerns aim to establish healthier body image, thus reducing the psychological distress associated with slight weight gain. CBT for cessation-related weight gain draws from treatments for eating disorders and body image disturbances and helps patients learn to modify maladaptive thoughts that lead to unhealthy weight control. Examples of these maladaptive thoughts include overvalued ideas of the importance of thinness, and all-or-nothing thinking (e.g., that one can be only thin or overweight, or there are good and bad foods). CBT may be particularly effective as a supplement to standard treatment for women who are weight-preoccupied.

Pharmacological Treatments. Certain medications may be especially helpful for weight-concerned smokers by helping to reduce weight gain. Bupropion is an antidepressant (selective reuptake inhibitor of dopamine and noradrenalin) that is an efficacious treatment for smoking cessation. Theorized mechanisms of its effectiveness in assisting smoking cessation include its antidepressant effects and its effectiveness in reducing nicotine cravings. Bupropion also reduces appetite for food, and may effectively curb weight gain following cessation, thereby increasing the likelihood of prolonged abstinence. Research has shown that smokers experience heightened food reward following smoking cessation and that bupropion effectively attenuates this increase. Research reviews indicate that bupropion is an effective and well-tolerated first-line treatment for smoking cessation. Naltrexone hydrochloride is an opiate antagonist and may be particularly effective for reducing post-cessation weight gain due to its regulation of appetitive behaviors. When administered in conjunction with the nicotine patch, low-dose naltrexone results in less post-cessation weight gain.

Smoking cessation is associated with modest weight gain. The exact mechanism of weight gain is not fully understood but is likely a combination of physiological and behavioral factors. There is some evidence that weight-preoccupied smokers have a more difficult time quitting due to their unwillingness to tolerate minimal weight gain. Although concerns about weight gain are more common for female smokers than male smokers, a significant portion of male smokers also report fear of cessation-associated weight gain. Treatments that address weight gain may be more successful for some individuals, especially those with heightened concerns about weight gain, and may increase interest in making a quit attempt.

See also **Advertising and Tobacco; Nicotine Delivery Systems for Smoking Cessation; Treatment, Behavioral Approaches to: Cognitive-Behavioral Therapy.**

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TOBACCO, ADVERTISING AND.

See **Advertising and Tobacco Use.**

TOLERANCE AND PHYSICAL DEPENDENCE.

In physical dependence, the brain and body chemistry undergo changes to adapt to the consistent presence of the drug, and this adaptation causes withdrawal symptoms if the concentration of the drug present is sharply reduced or removed altogether. Withdrawal symptoms are determined by the type of drug upon which the individual has developed physical dependence, but they are consistent for specific substances. That is, withdrawal from opioids is different than withdrawal from antidepressants or amphetamines, but withdrawal from a particular type of drug is consistent across individuals. So, the signs and symptoms of withdrawal from a specific substance will be largely consistent across persons who are physically dependent on it but may vary somewhat in terms of severity, speed of onset, and duration of effects.

As a rule, withdrawal symptoms are opposite of the drug's effects on the central nervous system: If physical dependence produces drowsiness, calm, and constipation, withdrawal will likely include agitation, insomnia, anxiety, and diarrhea (among a constellation of other symptoms). Those physiological functions or chemical processes that are altered or suppressed by the drug will usually be hyper-stimulated during withdrawal. Because tolerance leads an individual to use progressively more of a substance to achieve the same effect, withdrawal symptoms will typically correlate with both the amount and length of use.

Physical dependence is distinct from addiction in that the person who is physically dependent often uses to reduce pain or maintain homeostasis—not necessarily to achieve intoxication or a high. Persons who use pain medication may become physically dependent on the drug in order to manage symptoms but might not overuse or wish to continue substance use if the source of the pain no longer exists. Persons who are physically dependent on a drug may not experience adverse impacts on their social, familial, or occupational functioning as a result of the substance use and may not exhibit the drug-seeking behavior (willingness to take risks, compromised functioning, or making unwise decisions) that is typically present in persons with substance addiction.

TOLERANCE

Tolerance is the process that occurs when a drug is repeatedly administered over time; the body becomes accustomed to its presence and experiences progressively less effect from the drug. As a result, the person needs to use progressively more

of the substance over time to achieve the desired effect, whether that effect is a *buzz*, a *high*, or simply a sense of relief from troubling symptoms (such as pain, anxiety, or depression). Tolerance and physical dependence are common consequences of drug self-administration. To understand and modify alcohol and drug abuse and the problems they cause, people need to recognize how tolerance and physical dependence determine drug self-administration. Some alcoholics, for example, can appear unaffected at blood alcohol concentrations that would prostrate most social drinkers. For these alcoholics, tolerance makes possible escalation in drug use and in medical and psychological problems caused by heavy drug use. In addition to being highly tolerant, alcoholics will probably be physically dependent on alcohol, though tolerance and dependence have been shown to be distinct in their neurobiology.

Tolerance has to do with habituation: Over time, the same amount of a substance produces less effect. To obtain the desired substance-use effect, it is therefore necessary to increase the amount of substance used. There are several different types of tolerance. Acute tolerance occurs with a single exposure to the substance. For example, alcohol-induced impairment can be greater when measured soon after drinking begins than when measured later in the drinking session, even at the same blood alcohol concentration. Functional tolerance occurs with substance ingestion over time and reflects the development of different mechanisms by the brain and body to compensate for prolonged exposure to the substance. For example, chronic drinkers of alcohol can appear completely sober after drinking an amount that would inebriate or even kill other individuals, despite having a blood alcohol level that greatly exceeds the legal limit for intoxication. Functional tolerance increases the possibility for physiological damage because the substance user may ingest amounts that cause considerable damage without being aware of any bodily changes.

Environment dependent tolerance develops over time when the individual always uses the substance in the same place, under the same or similar conditions, and with the same cues. Tolerance is increased, or occurs more rapidly, when all of the conditions around the substance use remain relatively constant. In contrast, environment independent tolerance occurs when an individual habitually consumes large amounts of a substance (typically alcohol) and becomes functionally tolerant, regardless of where the consumption occurs or under what circumstances. The latter form of tolerance develops more gradually than the former.

Some aspects of tolerance may be influenced by genetics. One study compared sons of alcoholic fathers with sons of non-alcoholic fathers on a variety of measures. The results indicated that sons of alcoholic fathers were generally less functionally impaired by ingesting alcohol than were sons of non-alcoholic fathers. It is thought that sons of alcoholic fathers are more apt to demonstrate acute tolerance while drinking than the sons of non-alcoholic fathers. The predisposition to be less impaired by alcohol consumption and to develop acute tolerance may be associated with a genetic propensity to drink more and to develop alcoholism.

PHYSICAL DEPENDENCE

Physical dependence is defined as a physiologic state of adaptation to a substance. The absence of this substance produces symptoms and signs of withdrawal. The withdrawal syndrome is often characterized by over activity of physiological functions that were suppressed by the drug and/or depression of functions that were stimulated by the drug. Physical dependence requires a period of exposure to the substance adequate to produce adaptation to its effects. The duration and extent of exposure required varies among different substances. In an individual who is physically dependent on a substance, sudden cessation or a dramatic reduction in substance use causes withdrawal symptoms. These are typically uncomfortable but may be life threatening at times. Depending on their severity, the withdrawal symptoms may motivate the individual to use drugs or alcohol to alleviate discomfort.

The withdrawal symptoms experienced by persons who are physically dependent on alcohol include the following: feelings of craving for alcohol, nausea, sweatiness, shakiness, and anxiety, along with elevated blood pressure, pulse, and temperature. Symptoms of alcohol withdrawal become evident within 6 to 24 hours of the last drink. At its extreme, withdrawal from alcohol is accompanied by delirium, referred to as *delirium tremens*, which can be life threatening.

Common symptoms of withdrawal from opioids include yawning, sweating, watery eyes, stuffy and runny nose, abdominal cramps, nausea and vomiting, diarrhea, extreme feelings of weakness, dilated pupils, goose bumps and chills, muscle twitching, muscle aches and muscle pains, anxiety, insomnia, rapid pulse, rapid and shallow breathing, and increased blood pressure. The length of time until withdrawal begins varies by type of opioid and how long it took to metabolize out of the body. For example, users of morphine (or any of its derivatives) or oxycodone generally begin to experience withdrawal symptoms within 6 to 12 hours after the last use, whereas persons who abruptly cease using methadone may not experience withdrawal symptoms until 72 to 96 hours after the last use. The more severe the physical dependence, the longer lasting and more uncomfortable the withdrawal symptoms.

Persons who are physically dependent on benzodiazepines experience very similar withdrawal symptoms to those with alcohol dependence, but they are significantly longer lasting. Symptoms commonly associated with benzodiazepine withdrawal are anxiety and depressed mood. The major medical risk to individuals withdrawing from benzodiazepines is increased likelihood of having a seizure. People who use short-acting benzodiazepines experience withdrawal more rapidly than those who use long-acting varieties.

Between 1998 and 2008, researchers determined that withdrawal syndrome occurs with abrupt cessation of antidepressants, though these drugs are rarely abused. The withdrawal symptoms experienced by individuals physically dependent on antidepressants typically include acute anxiety and panic, followed by feelings of depression and (sometimes) suicidal ideation.

The general principle guiding the treatment of withdrawal is to use a long-acting substance from the same class (e.g., an opiate such as buprenorphine for heroin withdrawal) or a medication with similar pharmacological effects (e.g., a benzodiazepine for alcohol withdrawal) to suppress withdrawal symptoms. The medication dose is then gradually reduced, giving the body and brain adequate time to adjust to the drug's elimination.

See also **Addiction: Concepts and Definitions; Research, Animal Model: An Overview; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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TOUGHLOVE. The generic term *toughlove* (or tough love) describes a style of caring applied in diverse interpersonal contexts whereby one person or group reasserts power over another for whom he or she is responsible. Claire Kowalski was the first person to use the term in published material in 1976, to differentiate a respectful means of caring for elderly people that preserves self-mastery from a smothering style that promotes dependence. Since that first use, others have found the term useful. The Association of the Relatives and Friends of the Mentally Ill endorses the concept (Roberts, 1985). In its most common use today, the term describes the means by which parents of abusive, delinquent, or drug-abusing children can regain parental control. Toughlove is also the name of a self-help program for these parents and their children.

Toughlove, the self-help program, was developed by Phyllis and David York in 1980. They found that rescuing their daughter, who engaged in highly destructive behavior, did more harm than good. Instead, they permitted natural and logical consequences to correct their daughter's behavior while they sought emotional support from their friends. They wrote and published *Toughlove* (1980) and founded an organization called the Toughlove Support Network (which is described in their later book, 1984). The network's mission is to promote what they view as a mode of intervention for individuals, families, and communities.

According to the Toughlove philosophy, parents are the ones with the dominant power in a family. Children misbehave when parents fail to assert themselves or to take responsibility for their role as parents; but when parents' expectations are stated clearly, a child will no longer control the family. Parents are urged to describe the behavior they expect from their children. Speculation about the causes of child misbehavior is discouraged. Parents do not need to understand why their child misbehaves. Instead, they must act in coalition with other parents to assert control of themselves and their home environment.

Toughlove parents are taught not to feel guilty about their child's misbehavior because children are responsible for their own actions. A Toughlove parent of a destructive child might say: "We have had enough. We are not rescuing you from the trouble you have caused. We love you enough to say no." Proponents of Toughlove believe that drug and alcohol abuse is the most important causative factor in the disruptive behavior among teens. Once parents suspect drug and alcohol abuse, it is important that they investigate by questioning their child's friends, school officials, other family members, and anyone else their child meets frequently. When parents find drug and alcohol abuse, they must require abstinence. Strict discipline and limit setting are seen as the only means of enabling children to behave and to have a chance of regaining control of their lives.

Parents must confront their child about the drug and alcohol abuse and stipulate the behavior they expect. Toughlove recommends that they require the child to stop using drugs and seek treatment if needed. If a child refuses to comply, he or she is to be ejected from the home. Many uncooperative children are sent to live with another Toughlove family until they are serious about meeting their own parents' stipulations. Children who refuse to live with another Toughlove family are out on their own until they agree to their parents' rules.

To gain help in maintaining firmness and setting appropriate rules, parents attend a support group consisting of other parents who endorse the Toughlove principles. Toughlove support groups are organized by the parents without any professional leadership. Besides providing support for parents, Toughlove groups evaluate the effectiveness of

treatment programs and the effectiveness of professionals who treat children for alcohol and drug abuse.

Hollihan and Riley (1987) used qualitative research methods to study a Toughlove parent group. They found that several themes characterized group sessions and defined the Toughlove program experience for parents. First, the lay-led group emphasized that old-fashioned values are superior to those inherent in more permissive methods of raising children. Second, members regarded child-development professionals as advocates for modern child-raising methods that blame parents for child misbehavior. Third, they described the Toughlove group as their island of support within a pro-child social environment made up of the police, educators, social workers, and the courts. Last, the group provided successful models of rule setting by parents and enforcement of strict discipline—including as a final resort forcing a child to leave home. The group presented a persuasive and comforting rationale for the use of strict discipline that addressed the needs of parents who were experiencing great stress and feelings of failure (Hollihan & Riley, 1987).

Toughlove has been criticized as being simplistic and heavy-handed. According to Hollihan and Riley (1987), parents in the group they observed who did not believe their child was abusing drugs or alcohol were nevertheless instructed in ways to document such abuse. Other possible causes of their child's misbehavior were ignored, because the Toughlove solution is supposed to apply in all situations. The tactic of throwing an unruly child out of the house is especially controversial. Although most children go to live with other Toughlove families, some are forced to leave with nowhere to go and can become homeless, a predator or a victim, or a threat to themselves and others. For example, John Hinckley, who attempted to kill President Ronald W. Reagan in 1982, had been cast out of his home by parents who endorsed Toughlove and who later warned other parents to be cautious in disciplining their children.

Neither the Toughlove program nor the style of caring identified with it has been evaluated. On the one hand, there is anecdotal evidence from parents to vouch for it. On the other, as illustrated by the Hinckley family, Toughlove solutions can make matters worse. At present, we do not know whether the positive or the negative is the more common outcome, or whether positive outcomes result from factors having nothing to do with Toughlove.

See also **Adolescents and Drug Use; Parent Movement, The; Prevention, Education and.**

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TREATMENT

This entry includes the following essays:

AN OVERVIEW

The sections below cover a wide range of topics relative to the treatment of drug and alcohol problems. They are organized within 4 major subheadings. The first section, Behavioral Approaches, covers the range of *talk* therapies or psychotherapies as well as some of the common formats (long-term versus brief, group therapies). The next section includes articles on the major pharmacological strategies (medications) for treatment including newer approaches such as vaccines and long-acting (injectable) preparations. The third section covers specialty approaches (acupuncture, therapeutic communities) and populations (adolescents, older adults). The fourth section addresses treatment more broadly, reflecting the different stages of interventions and increasing the acceptance that addiction is a chronic, relapsing disorder similar to other chronic disorders such as diabetes and hypertension. This organization reflects the increasing recognition of commonalities across substance of abuse in terms of risk factors, co-occurring psychiatric disorders, and treatment approaches. Thus, treatments of specific drug and alcohol use disorders are covered within the major subheadings and to a lesser extent within the entries for each type of substance. In addition, brief overview sections that summarize the current state of knowledge on the treatment of alcohol and drug use disorders are included.

See also **Accidents and Injuries from Alcohol; Coerced Treatment for Substance Offenders; Criminal Justice System, Treatment in the; Substance Abuse and AIDS; Treatment: A History of Treatment in the United States.**

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AN OVERVIEW OF ALCOHOL ABUSE/DEPENDENCE

Early-twenty-first century treatment options for alcohol use disorders include psychotherapeutic interventions and medications. In addition, those individuals suffering from an alcohol use disorder can avail themselves of a unique network of self-help movements to support their efforts at recovery.

Besides the two broad types of interventions for alcoholism (psychotherapy and medications), treatment may be also conceptualized in terms of the phases or goals of the intervention. For example, this may include interventions whose primary goals are prevention and harm reduction, such as brief interventions for certain populations at risk, like college students, heavy drinkers, and adolescents or adults with additional psychiatric conditions. Interventions may also be aimed at acute stabilization, which might involve medically supervised inpatient care to stabilize and treat the alcohol withdrawal syndrome and any associated psychiatric or medical condition. Interventions aimed at maintenance and recovery may involve ambulatory care, and have short-term goals of reducing drinking behavior, achieving abstinence, and preventing relapse, and the long-term goals of recovery and health restoration. Typically, treatment is a combination of psychotherapeutic interventions, medication, and encouragement to become involved in self-help groups when feasible.

The self-help movement has a unique supportive role and tradition in the treatment of alcoholism. It emerged during the first half of the twentieth century as an independent self-help movement within the community of affected individuals (William, 1949; Khantzian & Mack, 1994). From that self-help tradition, empirically based psychotherapeutic interventions, such as twelve-step facilitation therapy and individual and group drug counseling, have evolved. These traditions have also enriched the treatment interventions by emphasizing broader elements related to recovery, such as promoting wellness behavior, spirituality, and personal growth. Self-help groups have, in addition, become more cognizant of the need to treat alcohol dependence with medication for a variety of reasons.

MEDICATIONS USED TO TREAT ALCOHOLISM

There are primary indications for which medications are commonly used in treating alcoholism. For the most part, they are used to treat alcohol withdrawal, to reduce or stop drinking behavior, and to treat associated psychiatric and medical conditions.

Medications for Alcohol Withdrawal. Alcohol withdrawal syndrome usually develops in people with a long history of sustained heavy drinking. This syndrome starts a few hours after such an individual stops drinking or attempts to reduce significantly his or her intake of alcohol. The syndrome may range in severity from mild anxiety, insomnia, tremors, and mild changes in vital signs,

to severe complications such as the development of alcohol withdrawal seizures and delirium tremens, with the latter still associated with a high degree of mortality if untreated. It is well known that the greater the number of previous withdrawals, the more severe the current withdrawal will be. The primary goals of the treatment of alcohol withdrawal syndrome are to prevent the severe complications mentioned earlier, to make the patient as comfortable as possible, and to help the patient address his or her alcohol problem and opt for follow-up treatment, as the phase of withdrawal may represent a window of opportunity, prompting the patient to commit to rehabilitation.

Benzodiazepine medications have been the standard treatment for alcohol withdrawal syndrome. Long- and intermediate-acting benzodiazepines are the most commonly used. Long-acting compounds allow less frequent dosing and produce a self-tapering effect, whereas intermediate-acting compounds with no active metabolites are the preferred medications in patients with compromised liver. In many settings, a withdrawal assessment scale is used in combination with medication to provide more comprehensive monitoring of the withdrawal syndrome and to guide medication dosing. Anticonvulsant medications, such as carbamazepine, sodium valproate, and gabapentin, are being used increasingly for the treatment of alcohol withdrawal. Preliminary research suggests that these medications may also be helpful in decreasing alcohol use subsequent to withdrawal, especially in people who have experienced previous episodes of alcohol withdrawal (Malcolm et al., 2002).

Medications for Reducing or Stopping Drinking Behavior. The U.S. Food and Drug Administration (FDA) has thus far approved three medications to treat alcoholism: disulfiram, naltrexone (both oral and intramuscular forms), and acamprosate. A number of other medications have also been tested, and some of them, such as topiramate, have shown efficacy in well-designed studies. Following is a brief description of the medications used to reduce or stop drinking behavior:

- Disulfiram is known as an aversive, or alcohol-sensitizing, agent. Aversive agents are compounds that produce a toxic reaction if alcohol is consumed. Disulfiram blocks the breakdown of ethanol by irreversibly inhibiting the enzyme aldehyde dehydrogenase (ALDH), which is responsible for the metabolism of acetaldehyde, a toxic by-product of alcohol. The resultant accumulation of acetaldehyde in the blood produces what is termed as the disulfiram-ethanol reaction (DER). The DER develops within a few minutes and may last 30 minutes or more. It ranges in severity from mildly increased heart rate and blood pressure, chills, nausea, vomiting, hypertension, and shortness of breath to moderate, and in some cases extreme, severity with convulsions, congestive heart failure, and cardiovascular collapse. The severity of the syndrome also depends on the dose of disulfiram and the amount of alcohol ingested. Disulfiram is useful in the treatment of alcoholism in a select group of patients, especially those with supervised medication ingestion. Disulfiram, like most medications, produces side effects; including worsening of psychotic symptoms. Calcium carbimide is another aversive agent. However, it is not available in the United States.
- Naltrexone is a pure, reversible opioid antagonist, approved by the FDA, initially for opiate dependence, and subsequently for alcohol dependence; it is available in oral and long-acting (1-month) intramuscular injection forms. This medication decreases drinking by reducing the positive reinforcing effect of alcohol. Studies have shown that naltrexone decreases drinking, improves abstinence rates, reduces craving, and therefore reduces the risk for relapse. Patients who continue to drink alcohol while on naltrexone report experiencing less of a "high." Naltrexone appears to reduce the desire to drink in alcohol-dependent patients as well as social drinkers. Multiple studies, but not all, have demonstrated the efficacy of naltrexone in its oral form when taken on a daily basis. Studies have also shown the effectiveness of targeted naltrexone use among problem drinkers to reduce their heavy drinking (Kranzler et al., 2003). In such a targeted scenario, the drinking patient takes naltrexone only in anticipation of exposure to a high-risk situation for heavy drinking. An intramuscular monthly injection of naltrexone (at a dosage of 380 milligrams) was also found effective in reducing alcohol use (Garbutt et al., 2005). In addition, naltrexone appears to be effective in combination with different

psychotherapies, including cognitive-behavioral therapy (CBT), supportive treatment, and medication management therapy (Anton et al., 2005, 2006). Nalmefene is another opioid antagonist, one which has been much less studied than naltrexone, and evidence of its efficacy in treating alcoholism is mixed, with some studies showing it to be efficacious and one other showing it to be no better than placebo.

- Acamprosate or calcium acetyl homotaurinate is the third FDA-approved medication for treating alcoholism. This medication decreases alcohol use by reducing the negative reinforcing effect of alcohol. Acamprosate is thought to normalize the glutamatergic excitation that occurs during alcohol withdrawal and early abstinence, leading to a reduction in craving, distress, and the need to consume alcohol. Several European trials have shown that acamprosate approximately doubles the abstinence rate over a 12-month period compared to a placebo, although studies in the United States have not shown it to be superior to placebo. Acamprosate is not metabolized in the body; it is excreted primarily by the kidney. It also has a good safety profile, with the main side effects being headache and diarrhea.
- Topiramate is an anticonvulsant medication approved by the FDA for the treatment of certain forms of seizure disorders and for the prevention of migraine headache, but not for alcoholism. It has been hypothesized that topiramate decreases the craving for alcohol and its rewarding effect by facilitating gamma-amino butyric (GABA) neurotransmission and dampening glutamate-related excitatory effects. Two rigorously conducted, double-blind, placebo-controlled studies; one single-site and one multisite; demonstrated the efficacy of topiramate in treating alcohol dependence (Johnson et al., 2003, 2007). A salient feature of these studies is that patients were still drinking a large amount of alcohol when the study drug was started. Thus, topiramate has proven efficacious in treating patients who continue drinking, and a period of abstinence is not required before starting the medication. Preliminary evidence also points to the usefulness of other anticonvulsants, such as sodium valproate, carabamazepine, and gabapentin, in decreasing alcohol use.
- A number of medications that affect the serotonergic system have shown efficacy in a subgroup of patients. For example, a low-risk low-alcohol severity subgroup was found to respond better to the antidepressant sertraline than placebo (Pettinati et al., 2000), whereas those with early-onset alcoholism (below the age of 25 years) responded better to ondansetron than placebo (Johnson et al., 2000).

Medications for Comorbid Psychiatric Disorders. Additional psychiatric difficulties such as major depression, bipolar disorder, anxiety disorders, or psychotic disorders requiring medication are often encountered among patients suffering from alcoholism. Several antidepressants have been tested on patients with major depression and alcoholism with mixed results, particularly in terms of the effects on drinking. A reduction in drinking was most evident in those groups that had experienced the greatest improvement in depressive symptoms.

Few studies have been conducted among subjects with both bipolar disorder and alcoholism. Sodium valproate was found effective in decreasing heavy drinking in this population (Salloum et al., 2005), but a recent controlled trial reported that quetiapine was no better than a placebo in improving the alcohol outcome (Brown et al., 2008). Paroxetine, a serotonin reuptake inhibitor, appears to be helpful in treating the symptoms of anxiety but not in decreasing alcohol use among patients with alcoholism and anxiety disorders. Open-label, follow-up studies have reported an improved alcohol outcome for patients with schizophrenia and alcoholism who were taking clozapine.

PSYCHOTHERAPY FOR ALCOHOL DEPENDENCE

There are many modalities of psychotherapy, and diverse techniques and theoretical approaches available to intervene in alcoholism. These include individual, group, and family therapy formats as well as self-help groups, all of which could take place with different intensity and frequency, in diverse treatment settings such as inpatient, residential, and ambulatory programs. Many therapeutic approaches have also been developed, including dynamically oriented psychotherapy, cognitive behavioral therapy (CBT), relapse-prevention therapy, motivational enhancement therapy, contingency management

therapy, network therapy, and disease management/medication adherence therapy. Furthermore, a number of these therapies have been empirically tested in large multicenter, randomized trials. Overall, although there is good evidence that the use of such psychosocial interventions is superior to no or minimal treatment, there is only limited evidence that one type of intervention is superior to the others.

A combination of psychotherapy and pharmacotherapy has also been studied in randomized controlled trials. Different manual-guided therapies for alcoholism, such as CBT, motivational enhancement therapy, and twelve-step facilitation therapy, among others, have been found effective in reducing alcohol use. Some therapies may be more apt to yield a better outcome than others. For example, exposure to the twelve-step facilitation therapy in Project MATCH (Project MATCH Research Group, 1998), a large multicenter study of psychotherapies for alcohol dependence, produced a higher abstinence rate at follow-up (Miller, 2005). The combination of psychotherapy and medication may be associated with improved outcome (O'Malley et al., 1992; Anton et al., 2005). For example, in the COMBINE study (Anton et al., 2006), as of 2008 the largest pharmacotherapy trial conducted to study alcoholism in combination with psychotherapy, showed that a combination of disease management therapy with naltrexone was among the most effective treatment of nine different kinds of treatment assignments.

Furthermore, brief interventions for alcoholism have been extensively studied and found effective in decreasing alcohol use among samples of drinkers with alcohol-related problems, including individuals who were not seeking treatment (Moyer et al., 2002; Vasilaki et al., 2006). Brief interventions appear to be effective when they are delivered using available technologies like telephone counseling or Web-based counseling (Blow et al., 2006; Mello et al., 2008). The key advantage to using such an alternative technology is the ability to reach a wider audience of affected individuals at a lower cost.

See also **Accidents and Injuries from Alcohol; Treatment: A History of Treatment in the United States.**

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AN OVERVIEW OF DRUG ABUSE/DEPENDENCE

Drug addiction is a medical and public health problem that affects everyone, either directly or indirectly. It has been estimated that drug abuse and addiction cost the United States more than $110 billion per year. If one adds the cost of nicotine to this figure, the number dramatically soars. Added to the economic costs are the personal, family, and medical problems associated with smoking and the use and abuse of other drugs. Improved prevention and treatment are the best ways to reduce all of these problems. Fortunately, advances in science have revolutionized the fundamental understanding of the nature of drug abuse and addiction and what to do about it.

Extensive data show that addiction is eminently treatable if the treatment is well delivered and tailored to the needs of a particular patient. An array of both behavioral and pharmacological treatments can effectively reduce drug use, help manage drug cravings, prevent relapses, and restore people as productive members of society.

Three decades of scientific research and clinical practice have yielded a variety of effective approaches to drug addiction treatment. Extensive data document that drug addiction treatment is as effective as treatments for most other chronic medical conditions. In spite of scientific evidence that establishes the effectiveness of drug abuse treatment, many people believe that treatment is generally ineffective. In part, this is because of unrealistic expectations. Many people equate addiction with simply using drugs, and they therefore expect that addiction will be cured quickly and permanently, so they view treatment as a failure if it is not. In reality, because addiction is a chronic disease, the ultimate goal of long-term abstinence often requires sustained and repeated treatment episodes.

Drug-abuse treatment programs using medications and/or behavioral techniques can and do work. The most successful treatment programs are a complex mix of medical, psychosocial, and rehabilitation services, including the use of self-help groups like Narcotics Anonymous and Cocaine Anonymous that attempt to deal with the unique needs of each individual. However, effectiveness of treatment can differ because of complex variables such as the type(s) of drug(s) to which a person is addicted, the dysfunctional lifestyles of many addicts, and time and treatment resources available to both addicts and treatment personnel. Many Americans affected by drug addiction have been restored to healthy and productive lifestyles through appropriate treatment.

NEW AND IMPROVED TREATMENTS

The National Institute on Drug Abuse (NIDA) has already made considerable progress in developing a variety of effective behavioral and pharmacological addiction treatments and making them widely available to the public. For example, NIDA has taken the lead in developing readily available nicotine addiction therapies. They have also brought to the world the most effective medications to date for heroin addiction, including methadone and buprenorphine and have standardized behavioral

interventions that have been effective in treating both adults and adolescents.

NIDA supports research to develop additional new and improved pharmacological and behavioral treatments. To this end, NIDA sponsors both a medications development program and a behavioral therapies development program. The NIDA medications development program brings the critical mass of knowledge of medicinal chemistry, molecular biology, brain function, and behavior to bear on the urgent public health problem of drug addiction to provide new medications as an effective adjunct to conventional psychosocial treatment by helping to stabilize addicts and allow them to succeed in their overall treatment program. Specifically, new medications are being researched to:

- block the effects of abused drugs;
- reduce the craving for abused drugs;
- moderate or eliminate withdrawal symptoms;
- block or reverse the toxic effects of abused drugs;
- or prevent relapse in persons who have been able to initiate abstinence (e.g., through medical or other means).

Because psychosocial interventions are the most common and sometimes the only treatments administered to individuals with drug addiction, NIDA also has a robust behavioral therapies development program to complement its medications portfolio. Researchers are working to develop new behavioral treatments for drug abuse and addiction and enhance the efficacy of existing ones. Psychotherapies, behavior therapies, cognitive therapies, family therapies, and counseling strategies are among the approaches currently being studied under this program. Once these treatments are proven to be safe and effective in small trials, they are tested in larger and more diverse populations through the NIDA National Drug Abuse Treatment Clinical Trials Network. This network enables the rapid, concurrent testing of a wide range of promising science-based medications and behavioral therapies across a spectrum of real-life patient populations, treatment settings, and community environments.

CONCLUSION

Addiction is a treatable disease. However, there is no one-size-fits-all treatment program. Treatment, which is delivered in outpatient, inpatient, and residential settings, has been shown to be effective in reducing drug use, but the settings and modalities of treatment must be tailored to the individual's needs. Drug addiction treatment can include behavioral therapy (such as counseling, cognitive therapy, or psychotherapy), medications, or a combination of both. Behavioral therapies, such as cognitive behavioral coping skills treatment, offer addicts ways to cope with their drug cravings, teach them to avoid drugs and relapse, and help them deal with relapse if it occurs. Medications and self-help group participation can augment these beneficial effects. The best programs provide a combination of therapies and other services, such as referral to other medical, psychological, and social services, to meet the needs of the individual patient.

See also **Alcohol: Chemistry and Pharmacology; Clinical Trials Network; Drug Interaction and the Brain; Economic Costs of Alcohol and Drug Abuse; Funding and Service Delivery of Treatment; Heroin; Methadone Maintenance Programs; Myths About Addiction and Its Treatment; Narcotics Anonymous (NA); Research: Aims, Description, and Goals; Research: Developing Medications to Treat Substance Abuse and Dependence; Tobacco: Dependence; Treatment, Behavioral Approaches to: Cognitive Therapy; Treatment, Behavioral Approaches to: Cognitive-Behavioral Therapy; Treatment, Behavioral Approaches to: Couples and Family Therapy; Treatment, Behavioral Approaches to: Self-Help and Anonymous Groups; Treatment, Pharmacological Approaches to: Buprenorphine; Treatment, Pharmacological Approaches to: Methadone; Treatment, Specialty Approaches to: Adolescents; Treatment: Outpatient Versus Inpatient Setting; Treatment: An Overview; Treatment, Pharmacological Approaches to: An Overview; U.S. Government Agencies: National Institute on Drug Abuse (NIDA); U.S. Government: Agencies Supporting Substance Abuse Research.**

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A HISTORY OF TREATMENT IN THE UNITED STATES

The history of the treatment of alcohol and other drug problems is often assumed to be a straightforward story of progress—moralism, neglect, and brutality were displaced by scientific knowledge, medical activism, and professional civility. A view that the addict freely chose continued drinking and drug use was succeeded by an understanding of how a disease or disorder could overrule the capacity to choose.

This assumption is historically incorrect. First, it neglects the coexistence and mutual influence of views emphasizing free will or social or biological determinism. Although one view may have enjoyed greater influence at a given time, its competitors have never been vanquished. No generation has any more solved the puzzle of addiction than it has resolved the related enigmas of the relationship between mind and body, choice and compulsion. Second, it is equally incorrect to associate condemnation and neglect with the free-will position, or kindness and activism with the determinist perspective. The historical truth is more complicated.

As various studies have demonstrated, there is a tenacious American folk wisdom about addiction. Simply put, it goes as follows: While addicts experience a compulsion to take a drug, this develops as the result of repeated bad choices that are socially influenced; further, addicts can rid themselves of compulsion only by developing self-discipline, perhaps with some skilled influence in the form of treatment. Thus, in contemporary culture, and despite the modern message that "addiction is a disease like hypertension or diabetes," addicts are understood to be sick *and* immoral, blameless *and* culpable, free *and* determined. In the popular mind, and among treatment professionals, addicts are ambiguous characters.

The history of treatment in the United States reflects this cultural dilemma. Cultures limit the range of possible responses to a problem, and because they tend to change slowly in fundamental ways, to the extent that an important problem recurs or remains unsolved, the range of possible responses will be explored repeatedly as new generations search for fresh insights and effective methods of intervention. At various times, treatment has embraced exhortation and coercion, sermons and miracle drugs, democratic mutual aid, and autocratic professional prerogative—often simultaneously. This entry will emphasize enduring cultural tensions and the therapeutic pluralism that continues to reflect them.

This approach to bounding a very large subject has at least one serious drawback that needs explanation at the outset. Sociologists and political scientists, in particular, often distinguish between "culture" as a value-laden, meaning-making process and "structure" as a pattern of relationships that generates its own imperatives. For example, any successful political system reflects to some extent the values of those it represents, but governance is achieved through structured relationships and processes that translate diffuse values and ideas into relatively specific social practices. The various processes and constituencies involved in sorting through values, reasoning about priorities, considering technical problems and group interests, and fitting proposals to the demands of political survival are fundamental to a thorough understanding of the history of treatment. And yet considering these processes is a huge analytic task due to the complexity of the modern American state (with its bewildering field of interorganizational relationships involving several layers of government and substantial fragmentation within each layer) and the existence in the United States of the world's most elaborate field of nongovernmental organizations (NGOs) that both influence the policy processes and provide the services. Thus, although structural factors will be discussed here, this entry is of necessity not a history of policy, public administration, or competitive strife among NGOs. Humbly stated, it is an introduction to some of the overarching sources of ideas about treatment and the institutional forms it has taken.

By way of further introduction, choices about periodization and terminology also need to be clarified. Modernity has different meanings with respect to the treatment of habitual drunkenness and drug addiction. In the case of habitual

drunkenness, the modern era is traceable to the birth of Alcoholics Anonymous (AA) in 1935. In the case of drug addiction, the modern era begins with the introduction of methadone maintenance (for heroin dependence) in 1965.

The terms *alcoholism* and *alcoholic* date from the mid-nineteenth century, but they did not come into common professional use until the early twentieth century and were not embedded in the American vernacular until after the rapid growth of AA during the 1940s. The more common professional terms in the premodern era were *inebriety* and *inebriate*, but as these often were used to refer to a heterogeneous group now called *substance abusers*, the durable term *drunkard* is most appropriate when writing about this era. Similarly, the term *drug addict* was not in common use until the early 1900s. Before this time habitual users of drugs were known by terms that reflected their preferences: They were *morphinists*, *cocainists*, and so forth (even though the use of multiple substances was common). Sometimes, they were known more generally as *dope fiends*, but to speak generally and to avoid pejorative (if historically accurate) terminology, the term *drug addict* is most useful. The terms *addict* and *addiction* are acceptable when speaking of both habitual drunkards and drug addicts.

PREMODERN TREATMENT OF HABITUAL DRUNKARDS

Colonials and Americans of the early republic drank astonishing quantities of alcohol. Quite unapologetically, men, women, and children drank morning, noon, and night. Their food was fatty and salty, the water was unhealthy around settlements, and the land was full of fruits and grains that could be converted into fermented and distilled beverages for drinking and transport without spoilage to sometimes distant trading centers. For these and other reasons, we were, in the famous phrase of historian William Rorabaugh, "an alcoholic republic."

As transplanted from England around 1810, the early American temperance movement was indifferent to reclaiming drunkards. Led by clerics such as Lyman Beecher, the movement aimed principally to shore up the respectability of the wobbly postcolonial elite by redefining the proprieties concerning alcohol consumption and the requirements of self-possession and cultural stewardship. Over two generations, such efforts were remarkably successful. By the first state prohibition law in Maine in 1851, drinking distilled spirits, especially, had become disreputable among aspiring young people—not unlike cigarette smoking in the early twenty-first century—and the per capita consumption of alcohol had declined significantly. Throughout the nineteenth century—indeed, until the so-called wet generation that followed national Prohibition (1920–1933)—abstention from alcohol remained a hallmark of respectability among the Protestant middling classes. Even as of 2008, about one-third of American adults do not drink, and this abstinent minority is concentrated among the Protestant faithful.

Tradition of Mutual Aid. The organized, specialized effort to help habitual drunkards began with the Washington Total Abstinence Movement in 1842. The Washingtonian Movement stands at the head of a tradition of mutual aid that developed throughout the remainder of the century in close connection to American Protestantism, particularly its evangelical expressions. The Salvation Army, which traces its American incarnation to the mid-1870s, also falls in this line, as does AA and the many "Anonymous" fellowships it inspired.

Washingtonian societies were dedicated to sobering up hard drinkers, usually (but not always) men. The societies intended to foster a solidarity based on shared experience with suffering that transcended profound social divisions. (Unlike the kindred Sons of Temperance, they were neutral on the divisive question of prohibition laws.) Although some famous teetotalers such as Abraham Lincoln were members, the societies included the disreputable, the unlettered, and sometimes nonwhites and women as equals. Their motives were couched in terms of Christian charity, economic self-improvement, and democratic principles. They had, one might say, one eye on the Almighty and the other on His worldly goods.

The hallmark of mutual aid is the banding together of people in similar circumstances to help one another. (The popular term *self-help* is thus misleading.) The Washingtonians and their successors did not invent the methods by which they fostered solidarity and mutual support. However, in adapting the voluntary association to the reform of drunkards, the Washingtonians introduced new elements.

Owing its provenance to the revival meeting, the most striking and controversial (some found it distasteful) Washingtonian innovation was the confession of drunkards before their peers, and sometimes before a general audience. Its contemporary form is familiar: "I am Jim B., and I am an alcoholic," but the practice dates from Washingtonian *experience lectures*, forums for telling so-called drunkard's tales, stories of degradation, struggle, and redemption through sobriety that nowadays form a common literary trope. These introduced the drunkard's tortured inner life to the polite public. "You all know me and what I used to be," Salvation Army lecturers often began.

Some Washingtonian societies also established temporary homes, or refuges, for drunkards. These were places where drunkards could live for a short time while they sobered up and were introduced to the Washingtonian fellowship, whose members found them jobs and other necessities. A century later AA would reinvent this institution (the *recovery home*) as part of its twelve-step work—the commitment to help other drunks.

Although not continuous with these early refuges, beginning in Boston (1857), San Francisco (1859), and Chicago (1863), a number of formal inebriate homes were established to treat drunkards in the Washingtonian tradition of therapeutic temperance. Typically, these were small institutions (fewer than 50 beds), operated as private charities, sometimes under religious or temperance auspices. They relied on the voluntary cooperation of their residents and used temperance fellowship as a form of what is now called aftercare. They were located in urban environments and did not isolate their residents from community life. Although often superintended by physicians, residence rarely exceeded three weeks and medical treatment was considered important only in managing withdrawal symptoms or delirium tremens (DTs). The terms *disease* and *vice*, *cure* and *reformation* were used interchangeably, and sober outcomes were attributed to the influences of family, friends, and the fellowship, not to medical intervention. Inebriate homes practiced a profoundly social (and sometimes spiritual) form of treatment based on the belief that the human capacity for transformation was never extinguished, no matter how "despotic" the appetite for alcohol.

For those in the Washingtonian line, the source of such optimism was their belief in the presence of an immortal God in the human mind. The mind, they believed, was distinct from the brain and other corruptible flesh and formed in God's image. By the mid-1800s the image of God was far more benign and rational than the often wrathful, finally inscrutable deity of even the early 1700s. This gradual change in the conception of God owed much to the spread of the market as arbiter of economic affairs and social relations. The rigorous logic of the market reordered economics from the academy to the workshop. In its train, a disciplined, optimistic rationalism—and the ideas of moral progress and human perfectibility—suffused popular culture and theology.

At the same time, another form of rationalism, that of natural science, was pervading popular discourse and causing tumult in seminary and pulpit. Science did not overthrow religion so much as assume a place alongside it. For believers, scientific order was a wonder of the divine plan. The natural *laws of health*, as various rules of disciplined self-denial were known, were signals of divine intent, of God's ideas about right living. The drunkard was therefore both sinful and sick, having contracted the disease as the result of moral transgression. (A common analogy of the time was to syphilis; today some religious leaders speak similarly of AIDS.) Thus, although Washingtonians and their successors spoke of addiction as a disease—by which they meant an organically based compulsion—they also employed religious images, for they believed in the power of the divinely inspirited human mind to choose the rational good (total abstinence from alcohol) and to thus achieve health. In the Washingtonian tradition, the languages of morality and disease became assimilated, and remain so in the many contemporary Anonymous fellowships' claim that addiction is in part a "spiritual disease."

Although the Washingtonian Movement as such was defunct by 1850, Washingtonianism was extremely influential until about 1865. The tradition did not disappear, but in the decades following the Civil War (1861–1865), profound changes in American culture and society, and related changes in the temperance movement, blunted Washingtonian influence and gave new prominence to a competing philosophy of treatment and its attendant

practices and institutional embodiment. The philosophy was that of biological determinism or *somaticism*, and its institutional expression was the *inebriate asylum*.

Asylum Tradition. In 1810 Benjamin Rush, a Philadelphia physician, signer of the Declaration of Independence, and first formulator of a disease theory of addiction (although not the inventor of the idea), proposed "sober houses" for drunkards. However, Samuel Woodward, a Massachusetts insane asylum superintendent and temperance orator, was the father of institutional treatment based on a somatic explanation of habitual drunkenness. In a tract written in 1835, Woodward contributed two critical ideas to what would become the inebriate asylum movement of the nineteenth and early twentieth centuries. The first was that drunkards could not be treated successfully on a voluntary basis. The second, which flowed from the first, was that they needed legal restraint in a "well-conducted institution"—by which Woodward meant something like the insane asylum that he superintended.

The course staked out by Rush and Woodward had no institutional realization until an inebriate asylum subsidized by the State of New York opened in Binghamton in 1864. Another was opened in Kings County, New York, in 1869. In subsequent decades, pursuant to arduous promotion by the American Association for the Cure of Inebriates (AACI, founded in 1870), public inebriate asylums opened in Massachusetts (1893), Iowa (1904), and Minnesota (1908). Other jurisdictions chartered inebriate asylums but never built them (Texas and Washington, D.C.). Indeed, Binghamton was converted to an insane asylum in 1879. By the advent of Prohibition in 1920, all public inebriate asylums had been closed or converted to other use. Prevention, it seemed, would be the cure.

The inebriate asylum movement spawned dozens of private sanatoriums that treated well-to-do drunkards and, by the 1890s, drug addicts. (The most famous of these—the Betty Ford Clinic of its day—was the Townes Hospital in New York City.) However, judged by its manifestation in brick and mortar, the movement for public treatment was a failure.

For two related reasons, the AACI was notably unsuccessful in converting legislatures to its cause. First, its physician members never could produce a strictly medical "cure" for addiction. Although its theorist-practitioners developed rigorously somatic explanations of addiction that dispensed with will power, spirituality, and the therapeutic necessity of fellowship, they relied on recuperation by bed rest, a healthy diet, and therapeutic baths (hydrotherapy), followed by the discipline of useful labor. This regime was highly structured (military analogies were popular), medically supervised, and set in a context of prolonged legal restraint (involuntary commitment). However, there was nothing particularly innovative or medical about this approach. Its methods already were the staples of lunatic asylums (called mental hospitals in most states after about 1900), almshouses, and county jails, institutions that managed huge numbers of habitual drunkards and, after the 1880s, drug addicts. Second, the inebriate asylum was an ambitious undertaking: Like the insane asylum, it was to accommodate several hundred patients on a sequestered rural estate. Few legislatures could be persuaded that such costly new institutions were worth the price. In a word, the inebriate asylum was viewed as redundant.

The ideology of the inebriate asylum movement—its adherents' view of the world—was shaped by two profound, contemporaneous developments in American culture and society: (1) the rising esteem and secularism of science and (2) the growing disorder and complexity of American society after the Civil War. The movement reflected the grand aspirations of Gilded Age science, whose practical applications were transforming American life: railroads and streetcars, the telephone, gas and electrical lighting—all attested to the power of science and human ingenuity. It was a time when "scientific" understanding became the basis for professional status for all manner of occupational groups, from proto-social workers to plumbers. The metaphor of disease and the optimistic message implicit in its use—that all defects could be cured—became popular among forward thinkers. In the most widely read book of its time, the utopian novel, *Looking Backward* (1888), Edward Bellamy characterized all sorts of misconduct as disease, and his near-perfect world of the year 2000 cured its rare wayward citizens in public hospitals.

If Washingtonians assimilated the languages of morality and disease, the rising generation of inebriate asylum enthusiasts radically separated them and

often reduced human volition to a by-product of neurology. (In the work of George Miller Beard, human nature had more in common with an electrical circuit than the image of God.) In the United States and Europe, they initiated research on the biology (and later, the genetics) of addiction. Primitive by early-twenty-first-century standards, it nonetheless established a robust tradition of inquiry that remains lively and influential.

The inebriate asylum movement appealed to American aspirations to create a better world through science, but it also addressed growing fears of social disorder. The extent of such disorder should not be exaggerated, however; preindustrial America was more disorderly than nostalgic chroniclers have made it seem, and urbanization and industrialization were less chaotic than critics sometimes contend. On the whole, though, life after the Civil War was more complex, more anonymous, and less certain.

Immigration from abroad was an important fuel for such change and promoted nativist fear. In the 1830s free Americans were overwhelmingly Anglo-Saxon in origin and Protestant in belief. By the 1880s this was changing dramatically. Burgeoning northern and western cities were becoming testing grounds for the promise and limits of diversity—indeed, for explanations of diversity. Amid glaring inequality of wealth and opportunity, cultural conflicts often were played out around practices of consciousness alteration. Protestant, native-born Americans (including African Americans) were remarkably abstemious (a notable success of the Protestant-driven temperance movement); the mostly Roman Catholic Italians and French were daily wine drinkers; Poles, Germans, and some Scandinavians drank large quantities of beer (some on Sunday—in public beer gardens, no less!).

Of Irish Catholics, who had a large temperance movement of their own but also a penchant for drunkenness (what is known as a *bi-modal distribution* of drinking habits), a California temperance editor wrote in 1883: "They are by far the worst and meanest material in which to store whisky." Native Americans had been introduced to alcohol by traders and government agents from colonial times, and the corruption of indigenous ways by whisky became a factor in the appropriation of western tribal lands and the ensuing Indian Wars. The "idolatrous" (non-Judeo-Christian) Chinese introduced opium smoking to America, a practice that crossed the color line during the 1870s and became popular among young white men and women during the 1880s. Then from 1900 to 1920 Mexicans became associated with marijuana use in the West and Southwest. In the South, African American men frequently were accused of the riotous use of cocaine, with subsequent designs on white women.

The increasing diversity of the U.S. population became a source of conflict and disorder; the continuing tempest of industrial capitalism was another. The United States experienced two prolonged economic depressions (then called *panics*) between the Civil War and the turn of the century—from 1873 to 1878 and from 1893 to 1898. In between, a short but sharp slump during the mid-1880s took its toll on stability. During these years the noun *tramp* entered the American language; the country experienced its first pronounced labor violence and political bombings (dynamite being an 1860s product of scientific ingenuity); in the spring of 1894 so-called armies of the unemployed converged on Washington, D.C., from all over the country.

This era of mounting diversity and instability was marked by a failing faith in exhortation as a method to achieve social regulation and by a concomitant exaltation of coercive means. Although never abandoning altogether its sympathy for drunkards, the temperance movement made securing prohibitionist measures its primary objective. Although never withdrawing their support from surviving Washingtonian institutions, temperance adherents simultaneously supported the more stringent regime promoted by inebriate asylum enthusiasts, some of whom believed that an orderly, peaceful society required the lifetime detention of incurable addicts. Indeed, the temperance movement helped to popularize theories that purported to demonstrate a biological basis for the failure of certain racial and ethnic groups to live up to the abstemious standard of so-called native stock—or to benefit from treatment. In the name of prevention, such views justified not only prohibition laws but also statutes that in a few states permitted the forced sterilization of addicts.

In sum, the legacy of the inebriate asylum movement was the biologically based approach to understanding addiction, the corollary claim that addiction is the special province of medicine and physicians, the notion that successful treatment requires legal coercion, and the assertion that treatment is both a responsibility of government and a commodity to be sold on the market. These ideas endure as part of the complex intellectual, professional, and political fabric of treatment.

Tradition of Mental Hygiene. The mental hygiene movement, customarily dated from the 1908 publication of Clifford Beers's *A Mind That Found Itself*, represented a departure from the somatic tradition of thought about mental disorder and addiction. At the same time, it did not appeal to spiritual explanations nor did it dwell on will power. Rather, mental hygienists employed a sociobiological determinism: Although addiction could be the result of hereditary biological defect and might be incurable, its origins were mainly familial and social, and if the condition was addressed early on, it could be arrested. Mental hygienists stressed the important roles of family, friends, and occupation in creating a salubrious environment for an addict's continuing sobriety. Mental hygiene did not speak the language of mutual aid, but it was similarly environmental in outlook. This was the beginning of what later would be called community mental health, and its point of view virtually defines what we understand to be "modern" about treatment and the biopsychosocial perspective.

The environmentalism of mental hygiene challenged the rationale of the asylum model of treatment. Mental hygienists criticized the asylum's lack of connection with community life and its reliance on involuntary treatment, claiming that only voluntary access to free or inexpensive care would attract patients in the early stages of drinking or drug-taking. The history of the Massachusetts Hospital for Dipsomaniacs and Inebriates (1893–1920) illustrates well the influence of mental hygiene philosophy and practice. Between 1893 and 1907 the hospital was run on the asylum model. After a complete reorganization in 1908, it followed a mental hygiene course: Most of its admissions were legally voluntary; the hospital established a statewide network of outpatient clinics; it worked closely with local charities, probation offices, employers, and the families of patients. Known finally as Norfolk State Hospital, it was a preview of what treatment would become beginning in the 1940s.

Even so, Norfolk created on its campus a "farm" for the long-term detention of so-called incurables. The mental hygiene movement modified the emphasis of the asylum tradition but did not entirely abandon its practices. Indeed, under the banner of mental hygiene, between 1910 and 1925, many local governments across the United States established farms to segregate repeated public drunkenness offenders and drug addicts. Some of these persisted until the 1960s, and some have been reopened in recent years to accommodate homeless people with alcohol and drug problems. As discussed below, the asylum tradition remained particularly important in the treatment of drug addicts.

PREMODERN TREATMENT OF DRUG ADDICTS

Although the San Francisco Home for the Care of the Inebriate (1859–1898) treated a few opium addicts as early as 1862, Washingtonian institutions mainly treated drunkards. The few reborn drug addicts among the legions of the Salvation Army and other urban missions were vastly outnumbered by reformed drunkards. Until the formation of Narcotics Anonymous (NA) in 1953, there was no large or well-defined group of addicts involved in the practices of mutual aid, and there were several reasons for this.

Drug addiction was not a matter of widespread concern until after the Washingtonian philosophy was eclipsed by the asylum model of treatment. Furthermore, drug addicts were quickly perceived to be more exotic and ominous than habitual drunkards. Although there were many people addicted to morphine as a result of ill-advised medical treatment or attempts at self-treatment during the late 1800s, this more or less respectable population declined after the turn of the century as physicians and pharmacists reformed their dispensing practices and new laws required disclosure of the content of proprietary (or patent) medicines and nostrums. At the same time, a growing number of urban young people began to experiment with drugs, especially smoking opium, morphine, and cocaine. By 1910 drug addiction was popularly

associated with petty thieves, dissipated actors, gamblers, prostitutes, and other nightlife aficionados, and with racial minorities and dissolute youth. Unlike habitual drunkards, drug addicts never were caricatured as boisterous and occasionally obstreperous nuisances or buffoons. Especially after 1900 they usually were portrayed as dangerous predators and corrupters of society, alternating between drug-induced torpor (in the case of opiates) or hyperactivity and hallucination (in the case of cocaine) and a craving that propelled them on relentless and unscrupulous searches for drugs and the means to buy them.

The "criminal" taint of drug addiction made mutual aid risky for participants, and the widespread view that most addicts were incurable and would do anything to alleviate withdrawal symptoms provided a powerful rationale for their prolonged confinement under strict conditions. Even the mental hygienists at Norfolk State Hospital had no expectation that addicts would remain sober and favored incarcerating them in the Massachusetts State Farm at Bridgewater, a correctional facility. Indeed, state hospitals were generally more opposed to admitting drug addicts than habitual drunkards, preferring to have them incarcerated in jails. Even more than drunkards, addicts disturbed the routine and good order of state hospitals, in no small part because they were, as a group, considerably younger and less conventional than other hospital patients. They pursued sexual liaisons in violation of institutional rules against fraternization; they smuggled drugs into the hospitals; and once through withdrawal, they escaped in droves.

Nor were jails and prisons anxious to take in addicts, mainly because of the problem of smuggling. By the 1870s opium was a customary (although illicit) medium of exchange at San Quentin Prison in California, and it was routinely available in the big county jails of the United States at the turn of the century.

As state laws against the sale or possession of opiates and cocaine proliferated in the 1890s, and as they began to be more strictly worded and enforced after 1910, county jails and state prisons faced a major problem of internal order. This intensified with the implementation of the federal Harrison Narcotics Tax Act (passed in 1914 to take effect in March 1915), particularly after a U.S. Supreme Court decision in 1919 made it illegal for physicians to prescribe opiates for the purpose of maintaining an addict's habit. The vast majority of drug offenders, even those arrested by federal agents, were prosecuted under state drug and vagrancy laws and sent to state and county lockups. The resulting crisis led jailers to support two related treatment strategies.

The first of these was the creation of special institutions for drug addicts. Thus, the aforementioned county farms were created, or laws were passed to allow addicts to be committed to existing state or county hospitals with wards designated for this purpose. Mendocino State Hospital in California, Worcester State Hospital in Massachusetts, Norwich State Hospital in Connecticut, and Philadelphia General Hospital, to name a few, treated significant numbers of addicts in the 1910s and 1920s. Later, California (1928) and Washington (1935) opened state-sponsored variations on the jail farm, although under the auspices of their state hospital systems.

Jailers were also important to local political coalitions in support of a short-lived and controversial treatment strategy of the early 1920s—drug dispensaries for registered addicts. At least 44 such clinics were established nationwide, most in late 1919 or early 1920, following the Supreme Court's antimaintenance ruling.

In principle, these were not to be maintenance clinics. Addicts initially were to receive their customary dosages of morphine (occasionally heroin and, very rarely, smoking opium) and were then to be "reduced" over a short time to whatever dosage prevented withdrawal. At this point, abstinence was to be achieved.

In practice, few of the clinics worked this way. Many clinic operators believed that their primary aim was to mitigate drug peddling by supplying addicts through medical channels. This implied a maintenance strategy at odds with the Supreme Court's interpretation of the Harrison Act and with some earlier state laws forbidding maintenance (in California and Massachusetts, e.g.). Furthermore, most clinic operators agreed with the American Medical Association that dispensaries could only work effectively within the law if prolonged institutional treatment was available once the addict's dosage had been reduced to the brink of withdrawal. In

the absence of such institutional capacity, reduction was useless, and so clinic doctors rarely bothered. The Prohibition Unit of the U.S. Department of the Treasury (which enforced the Harrison Act), state boards of pharmacy (which typically enforced state drug laws), and local medical societies and law enforcement agencies regarded the clinics as stopgaps, valuable only until adequate public hospitals could be opened.

In the midst of the inflation following World War I, localities looked to the states to finance such institutions and states looked to the federal government, particularly the U.S. Public Health Service, which had operated hospitals for merchant mariners since 1792. But the first proposed legislation to create a federal treatment program along mental hygiene lines failed to pass and the states were thrown on their own resources. The Prohibition Unit, convinced that the clinics were doing more harm than good, moved to close them, threatening dispensing physicians with prosecution. The clinics closed rapidly. The last one, at Shreveport, Louisiana, closed in 1923. Addicts were consigned to their customary ports of call in jails, prisons, or for the fortunate few, private sanatoriums.

The growing number of addict prisoners in the federal system also led to their segregation, first at Leavenworth, Kansas (mainly), and then at two narcotic hospitals opened at Lexington, Kentucky (1935), and Fort Worth, Texas (1938). (Women were sent to a federal prison in Aldersen, West Virginia, where singer Billie Holiday served time.) Operated by the U.S. Public Health Service, these hospitals were in fact more like jails, although they were authorized to admit voluntary patients of supposed good character whose applications were approved by the U.S. Surgeon General. Initially, these patients were kept involuntarily once they had been admitted, but a federal district court ruling in 1936 affirmed that voluntary patients could leave after giving notice. Before they were closed in the 1970s, the two facilities admitted more than 60,000 individuals, accounting for over 100,000 admissions.

The controversy over maintenance did not disappear, however, particularly on the West Coast, where efforts to loosen its prohibition in the states of California and Washington continued until the United States entered World War II in 1941. Furthermore, both federal and state governments permitted the maintenance of a small number of addicts, usually of middle age or older, suffering from severe pain related to a terminal illness or an incurable condition. However, the period from 1923 through 1965 was generally characterized by the strict enforcement of increasingly severe laws against drug possession and sales, by relentless opposition to maintenance, and by treatment that was essentially in the asylum tradition, supplemented by the mental hygiene innovation of supervised probation. In 1961 California passed legislation permitting the compulsory treatment of drug addicts (including marijuana users) and established the California Civil Addict Program within its Department of Corrections. From 1962 to 1964 more than 1,000 people were committed to a 7-year period of supervision, which typically involved an initial year of residential treatment in a facility surrounded by barbed wire to discourage premature departure. In 1964 New York passed similar legislation but assigned its implementation to a special commission rather than the Department of Corrections. As in California, New York's residential treatment facilities were "secure." As late as 1966, the federal Narcotic Addict Rehabilitation Act (NARA), in most respects a piece of modern legislation, nonetheless provided for the compulsory treatment of addicts and made the hospitals at Lexington and Fort Worth into the institutional bases of the NARA program.

THE MODERN ERA

The modern history of alcohol and drug treatment has been shaped by the therapeutic pluralism descended from the mutual-aid, asylum, and mental hygiene traditions; the coexistence of public and private sectors of treatment; and an increasingly complex field of interorganizational relationships involving several layers of government and myriad NGOs. As well, drugs with modest effects on consciousness (such as nicotine), and even pleasurable behaviors that have the potential to become obsessive (such as sex and gambling), are often brought together with drinking and drugging under the rubric of behavioral health problems.

Consolidating terms like *behavioral health* reflect important changes in the organization of treatment practices as well as the reorganization of the bureaucratic entities that fund and study intervention and

train practitioners. In the early twenty-first century substance abusers of all sorts are treated together in most programs (opiate maintenance is the obvious exception), but this is a development of the last 30 years. When in the mid-1970s a hospital in Pennsylvania advocated the joint treatment of alcoholics and drug addicts, the idea was controversial.

Although the accumulating insights of brain science and research on intervention provide reasons to treat substance abusers together (as well as some reasons to develop separate clinical regimes), the change on the ground probably originated in generational experience. Drugs other than alcohol are no longer exotic and their users and abusers have a more domesticated image. Even if they have not themselves been users, most Americans who have come of age after about 1970 know people who have been and some whose lives have been derailed by such use. Dabbling in various substances is now a commonplace experience of development, and choice of drugs is no longer such a reliable predictor of divisions among America's social worlds. The former antagonism in treatment programs between the "respectable" drunks and the "degenerate" drug addicts is no longer of much importance. The training of addiction specialists within the major human service professions and their separate licensing as addiction counselors in many states since the 1980s have institutionalized this change of perspective.

But access to treatment—like access to health care more generally in the United States—remains keenly divided by the existence and nature of job-related benefits. In 1990 the Institute of Medicine described U.S. treatment arrangements as a two-tiered system, composed of public and private sectors in which the private sector garnered a disproportionate share of expenditures. This characterization is as true in 2008 as it was then. To understand recent developments in treatment, it is important to understand some things about the history of this system.

A Two-Tiered System. By Repeal in 1933 nothing remained of the U.S. public treatment system save the specialty wards of a few state and county hospitals. Treatment was a commodity to be purchased by those who could afford it, and although few specialized private treatment institutions survived Prohibition, a number of private sanatoriums around the country treated alcoholics and addicts along with psychiatric patients. (The superintendents of these institutions did not like addicts as patients any more than physicians in public hospitals, but these patients or their families paid quite handsomely.) Before the 1960s, only the creation of the federal hospitals at Lexington and Fort Worth had much impact on public treatment capacity.

In addition, insurance companies worked assiduously to reduce their risk on life and disability policies by excluding known alcoholics or drug addicts. Abstainers were offered lower rates than drinkers, as nonsmokers are today. As health insurance developed within the industry, addiction treatment was systematically excluded from benefits due to skepticism about its efficacy and concerns about its cost.

Beginning in 1964 (with Kemper Insurance Companies), and expanding over the next decade to include a few insurance industry leaders such as The Travelers, health insurance policies began to provide coverage for the treatment of alcohol and drug dependence. Sometimes this was the result of industry investment in early detection intended to reduce long-term costs; sometimes it resulted from labor negotiations; sometimes it was the result of state insurance commission mandates for its inclusion. Whatever the impetus, in response to the availability of support, private hospitals (both nonprofit and for-profit) expanded their treatment capacities dramatically. There had been no such growth in the private treatment sector since the boom of the inebriate asylum era.

Commonly, treatment programs within the private sector were based on the Minnesota model, emphasizing twelve-step principles and employing recovering people. Such programs typically consisted of a brief period of inpatient detoxification followed by several weeks of inpatient rehabilitation. Twenty-eight days was such a common duration of inpatient care that the programs often were referred to as 28-day programs. The posthospital phase of treatment usually consisted of participation in AA, NA, or Cocaine Anonymous (CA).

Such programs—often called chemical dependency programs because they admitted people with drug *and* alcohol problems—catered almost exclusively to those with health insurance. (In many

instances, they represented important profit centers for medical institutions needing to subsidize financial losses from other services, such as emergency rooms.) Those without insurance either had no access to treatment or made use of the network of publicly supported programs—a network that became increasingly thin during the 1980s and increasingly under pressure to find sources of funds other than public grants and contracts and payments from medical programs for the indigent (such as Medicaid, established in 1965). During the 1980s sliding fee scales became more commonly used in public programs, and in some places scarce public treatment slots were absorbed by fee-paying drinking drivers mandated to treatment by stricter penalties for drunk driving and more systematic enforcement of such laws.

The growth of the private sector was spurred as well by employee assistance programs (EAPs), efforts to intervene in alcohol and/or drug problems at places of employment. This strategy goes back at least to the Washingtonian movement, but formal EAPs date from the 1940s, when wartime employers, faced with labor shortages, struggled to keep impaired workers on the job. Insurance companies such as Kemper and The Travelers were pioneers in EAP development during the 1950s and 1960s, and with insurance coverage available for treatment, the number of EAPs swelled during the 1970s and 1980s. Generally, EAPs referred people with more serious alcohol and drug problems to formal—usually private—treatment programs, which were paid primarily by fees derived from third parties such as insurance companies, who in turn derived their funds from policies paid for or subsidized by employers.

By the 1990s the ambitions of many private treatment programs fueled a constant search for clients and fierce competition among for-profit providers especially. Very quickly, the sharply rising cost to employers of providing alcohol and drug treatment became a major factor in the development of managed care, which was aimed initially at controlling the cost of mental health and alcohol and drug treatment. The major mechanism by which the managed-care industry addressed the cost of treatment was to challenge the practice of using several weeks of inpatient care as the initial phase of treatment for alcohol and drug dependence. In practice, treatment providers were told that inpatient treatment beyond a few days could not be justified by research and would not be paid for under the insurance policy.

The success of managed care in reducing costs by constraining the use of inpatient treatment resulted in a dramatic growth of managed-care organizations and an equally significant contraction and restructuring of the private alcohol and drug treatment system. By the early 1990s a number of states had obtained federal permission to use managed-care approaches to contain the costs of treatment for individuals covered by federal programs such as Medicaid. (Each state determines whether and to what extent alcohol and drug treatment is covered by its Medicaid program.) The result of this industry shake out and the adoption of cost-containment measures in the public sector radically altered available alcohol and drug treatment, as discussed below.

MODERN ALCOHOLISM TREATMENT

It is hard to exaggerate the influence of AA on the nature of modern treatment. Whatever its therapeutic success—a point of warm debate among scholars—AA has profoundly affected the treatment of people now regularly known as alcoholics. Indeed, AA and its Anonymous cousins have changed how recent generations think about the compulsive consumption of almost anything, from intoxicating substances to food or exhilarating experiences.

AA's impact has been both ideological and institutional; that is, its promotion of "disease theory" within the mutual-aid tradition has changed the perception of excessive or problem-causing consumption and treatment methods, and the penetration of policymaking bodies and treatment institutions by recovering people has shaped the funding and practices of treatment. The somaticist entrepreneurs of the inebriate asylum movement cast out sufferers as potential sources of therapeutic wisdom; AA brought them back.

AA's impact was facilitated by the growing influence of the mental hygiene movement during the 1920s and 1930s, for AA provided the critical therapeutic bridge between the segregating institution and the community at large. This was recognized quickly by men such as Clinton Duffy, the

"reform" warden of San Quentin, who encouraged the establishment of AA groups in his prison in 1942. Much early twelve-step work was done in U.S. county jails. Harvard psychiatrist Robert Fleming opined in 1944 that the prolonged institutionalization of alcoholics was no longer necessary; a week's medical care in a general hospital followed by community-based psychotherapy and AA participation was his new prescription. The growth of AA permitted the first substantial stirrings of community care since the Washingtonian Movement.

During the early 1960s some state hospitals, particularly in Minnesota, incorporated recovering alcoholics and the principles of AA into their treatment programs. What became known as the Minnesota model of short-term inpatient care and subsequent AA fellowship and recovery-home living spread slowly but discernibly among private treatment providers such as the Hazelden Foundation, also in Minnesota, and the Mary Lind Foundation in Los Angeles. Across the country, local councils on alcoholism, dominated by people recovering from alcoholism and encouraged by the National Council on Alcoholism (now, fittingly, the National Council on Alcoholism and Drug Dependence) and the National Institute of Mental Health (NIMH, created in 1946, was an ardent promoter of community psychiatry), began to press states and localities for outpatient clinics, diversion of alcoholics from jail, and other methods consistent with the traditions of mutual aid and mental hygiene. (Even so, a survey in 1967 found only 130 outpatient clinics and only 100 halfway houses and recovery homes dedicated to serving alcoholics, and alcoholics continued to be barred from most hospital emergency rooms.)

The intellectual warrant for such advocacy and organizing was E. M. Jellinek's *The Disease Concept of Alcoholism* (1960). Jellinek was more provisional in his use of the term than most of his readers appreciated, but he understood the important strategic value of such a claim. In the first instance, the language of disease challenged the legal and correctional system's jurisdiction over alcoholics; in addition, it provided a rationale for the increased availability of services within established medical facilities and under the aegis of public health. Several important court decisions in the 1960s endorsed the view that alcoholism was a disease. In 1967 a presidential commission on law enforcement concluded that it was both ineffective and inhumane to handle public drunkenness offenders within the criminal justice system and recommended creating a network of detoxification centers instead. In 1970 Congress passed the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment and Rehabilitation Act (the Hughes Act). This legislation made federal funds available for the first time specifically for alcoholism treatment programs.

The Hughes Act effectively redefined alcoholism as a primary disorder, not a symptom of mental illness. Based on this distinction, it created a federal agency—the National Institute on Alcohol Abuse and Alcoholism (NIAAA)—that would not be dominated by the mental health establishment competing for the same resources. NIAAA aggressively sought state adoption of the model Uniform Alcoholism and Intoxication Treatment Act. Section 1 of the Uniform Act stated that "intoxicated persons may not be subject to criminal prosecution because of their consumption of alcoholic beverages but rather should be afforded a continuum of treatment." By 1980, 30 states had adopted some version of the Uniform Act, thereby decriminalizing public drunkenness.

The thrust of federal and state grant making was to create an effective system of community-based alcoholism treatment services. This occurred in tandem with the deinstitutionalization process that was rapidly depopulating state mental hospitals. Although state hospital depopulation is customarily thought to affect only persons with mental illness, it had an important impact on alcoholics. In 1960, a decade before deinstitutionalization began in earnest, 36 states had provisions specifically for the involuntary hospitalization of so-called alcoholics, habitual drunkards, or inebriates. In addition, many states had voluntary admission statutes. By the mid-1970s, however, these laws were history. Prepared or not, local communities had to provide.

They did so within a unified substance abuse, chemical dependency, or behavioral health framework and the tiered system described above. With managed care, treatment became based almost entirely on outpatient measures supplemented by participation in an Anonymous group; long-stay

residential treatment became an experience for the rich, who could pay out of pocket. Moreover, because outpatient treatment typically was voluntary, initial and continuing participation rates declined. Whatever its therapeutic implications, lagging participation triggered more financial distress for treatment agencies, which looked to captive clients—that is, those mandated to treatment by criminal justice and child welfare authorities, mainly, and sometimes by employers using treatment as the carrot on the stick of workplace drug testing. Coerced treatment, once a matter of bitter controversy in AA, is now widely accepted in Anonymous circles as a means to "bring the bottom up"—that is, as a way to quicken the addict's disgust with his or her life.

MODERN DRUG TREATMENT

By the late 1950s the antimaintenance consensus of an earlier era of drug control and treatment was breaking down. A joint report of the American Bar Association and the American Medical Association in 1958 cautiously favored outpatient treatment and limited opiate maintenance as alternatives to "threats of jail or prison sentences." In 1962, appealing to disease theory, the U.S. Supreme Court struck down a California statute that made drug addiction per se a crime. Medical treatment, not the "cruel and unusual punishment" of incarceration, was the Court's desideratum. In 1963 the President's Advisory Commission on Narcotic Drug Abuse made substantially similar recommendations.

Although now supplemented by other maintenance drugs (including heroin in a few countries), the experimental success of methadone finally altered the discussion of opiate maintenance that had been quashed with the closing of the clinics from 1919 through 1923 and the prosecution of dissenting physicians in the years that followed. Methadone, a synthesized drug with opiate properties, was invented by German pharmacologists during World War II and had been used at Lexington to block addicts' withdrawal symptoms. In 1963 and 1964, with the support of the prestigious Rockefeller University, medical researchers Vincent Dole and Marie Nyswander began to study its wider use in the treatment of heroin addiction. Their research, first published in 1965, proceeded despite opposition by the federal Bureau of Narcotics. They observed remarkable changes in their patients that soon were replicated by other scholars. Methadone maintenance attracted considerable notoriety and generated new enthusiasm for maintenance as a strategy of treatment.

Nevertheless, methadone maintenance has never been without controversy. The fundamental criticism of maintenance—by whatever drug—has always been that it presumes "incurability," encourages users to continue to remain dependent on a drug, and thereby undermines abstinence-based approaches. During the 1960s, and especially during the 1970s, when methadone maintenance programs expanded rapidly, this criticism derived mainly from two sources: (1) abstinence-based programs run by recovering addicts more or less in the mutual-aid tradition and (2) African American and Hispanic poverty activists who saw in maintenance a palliative strategy to treat a symptom of economic deprivation without addressing its causes.

Opposition from those working in the mutual-aid tradition came chiefly from veterans of therapeutic communities inspired by Synanon (established in Southern California in 1958) and Daytop Village (opened in New York City in 1964). The term *therapeutic community* (TC) covers a wide range of practices that have changed considerably over the last 50 years as most TCs have become far more influenced by professional insights and standards, in part as the result of funding requirements. The common denominators among TCs, however, are the ideas that recovery from addiction involves a wholesale reconstitution of behavior, thinking, and feeling; that the processes of a community of residents are the treatment itself; and that abstinence from substances is the only desirable outcome. Unlike mutual aid in the Washingtonian tradition, TCs tend to carefully control their residents' participation in local communities. They are sometimes isolated worlds. Indeed, in one infamous case, Synanon became a separatist cult that sought legal standing as a religion. In this sense, then, the TC has some asylumlike characteristics, and "graduation" often marks a transitional process facilitated by an Anonymous fellowship.

Most therapeutic communities work in the assimilated languages of morality and disease, but from their beginning a few have also relied on an analysis of addiction that locates its social sources in adaptations to poverty. This was an important theme of much scholarship on drug addiction

during and after the late 1950s. In this analysis, still vital in the early twenty-first century, no form of treatment is effective without job and community development to support aftercare and prevent relapse. Descending from the mental hygiene tradition, this view provides a rationale for great skepticism about any narrow medical approach proclaimed as a solution rather than a first step.

There was (and remains) no inherent contradiction between maintenance and antipoverty strategies. In the 1960s many antipoverty workers embraced methadone as a viable and useful treatment. But many did not, and the result was an uneasy pluralism in drug-treatment approaches. In 1966, when New York City launched a major expansion of treatment for drug addiction, it chose to make drug-free therapeutic communities the centerpiece of its effort.

Despite the variety of approaches, accessibility to voluntary treatment remained limited to the federal narcotic farms and some state and local hospitals throughout the 1960s. The Narcotic Addict Rehabilitation Act of 1966 authorized NIMH to make grants to establish community-based treatment programs. The first of these grants was awarded in 1968; ecumenically, they provided federal support for therapeutic communities and methadone maintenance. This expansion of treatment capacity was also notable for its attention to problems associated with a variety of drugs. It came at a time of sharp increase in marijuana use among middle-class youth, an epidemic of amphetamine use, growing experimentation with LSD, and media preoccupation with the counterculture or "youth revolt." Thus, the political urge to provide treatment was fueled by two enduring concerns of Americans: unconventional and disorderly behavior by young people and minority group members; and the connection between drug use and crime.

For a short time in the early 1970s federally supported treatment expanded rapidly. Anything that might work was tried. In early 1971 there were 36 federally funded treatment programs in the United States. By January 1972 there were 235, and by January 1973 almost 400. This heyday did not last long, however. Buffeted by a terrible economy (the infamous period of stagflation and the near bankruptcy of several big cities, including New York), subsequent federal regimes allowed the real value of federal treatment spending to be eroded by inflation. Measured in 1976 dollars, the level of federal support for treatment was cut almost in half between 1976 and 1982. At the same time, as the result of the impact of inflation on the cost of state and local government, these jurisdictions also curtailed their support, thus aggravating the impact of federal reductions.

Since 1980 federal money for treatment has flowed to the states in the form of a *block grant*, a fixed sum that the states may spend as they see fit but within a set of federal priorities. Despite some increases in the amount of these grants, particularly during the second Clinton administration, access to public treatment remains constrained and dependent largely on the willingness of states and localities to supplement federal funds. Put another way, access to public treatment in the United States has a lot to do with where one lives. (A few states do not permit methadone maintenance.) Absent public treatment, access depends largely on one's health insurance. The federal Substance Abuse and Mental Health Services Administration found that from 2004 to 2006, among persons who needed but did not receive treatment for illicit drug or alcohol use, and made an effort to get it, 36.3 percent had no health insurance and could not afford the cost.

The future of treatment is inseparable from the broader debates on the financing of health care and the management of nonviolent drug offenders. California's Proposition 36 (the Substance Abuse and Crime Prevention Act of 2000) diverts nonviolent drug offenders to mandatory treatment and has saved the state hundreds of millions of dollars compared to previous business as usual in the prison system. Even so, the California approach has gaps and capacity problems and has faced some political opposition.

It remains to be seen what the balance of public and private treatment will be in the years ahead, what innovations or reinventions will be born of financial necessity, practical applications of neuroscience, or as the result of homeless addicts and a groaning correctional system. History allows one to predict the likely questions, but it is not a very reliable guide to specific answers.

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TREATMENT, BEHAVIORAL APPROACHES TO

This entry includes the following essays:

AN OVERVIEW

Behavioral treatments encompass a wide range of nonpharmacologic approaches to the treatment of substance-related problems. These approaches are also often referred to as "psychotherapy," "psychosocial approaches," "counseling," and "talk therapies." Behavioral therapies may be combined with other approaches (e.g., medications, case management), which are delivered in a range of settings (e.g., inpatient, outpatient, residential, and prisons) and at various stages of treatment (e.g., assessment, engagement, stabilization, aftercare). In addition, they can be delivered by a range of different clinicians, such as psychiatrists, psychologists, social workers, counselors, or ministers. Generally, however, behavioral treatment refers to an intervention wherein the individual meets with a clinician and, together, they determine the aims and goals of the intervention and the steps to be taken to reach those goals. They will both then monitor the individual's progress in meeting the established goals.

In general, although they vary greatly in their theoretical foundation, approach, and duration, well-defined, competently administered behavioral therapies tend to be associated with positive treatment outcomes. (Behavioral therapies that have been proven to work in clinical trials are often referred to as "empirically evaluated" or "evidence-based" approaches.) Further, retention in treatment is a key factor associated with improved outcomes. The sections that follow provide a survey, with a brief description and evidence for effectiveness, of some of the most commonly used and studied behavioral

approaches in the treatment of substance use and related disorders.

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COGNITIVE THERAPY

Cognitive treatment is based on the assumption that the way one thinks is a primary determinant of feelings and behavior. Developed from Beck's research (Beck et al., 1979, 1993), cognitive treatment is approached as a collaborative effort between the client and therapist to examine the client's errors and distortions in thinking that contribute to problematic behavior. This examination is fostered through a combination of verbal techniques and behavioral experiments to test the underlying assumptions the client holds about the problematic behavior.

Cognitive treatment in the substance abuse field was a direct extension of Beck's work. Beck's catalog of distorted thoughts examined in depression were found to be applicable to cognitive distortions and errors that accompany addictive disorders. Various cognitive treatments for substance abuse focus on these distortions and vary primarily in the techniques used to change these thought processes.

In relapse prevention (Marlatt & Gordon, 1985), cognitive distortions are viewed as instrumental in the process that leads to relapse. By helping the client thoroughly examine the thoughts that accompany substance use, therapy can reduce the likelihood of a lapse (single use), as well as help prevent a lapse from becoming a relapse (return to uncontrolled use). This is accomplished by examining the following cognitive errors:

1. Overgeneralizing—this is one of the most frequently occurring cognitive errors that helps a single lapse become a full-blown relapse. By viewing the single use as a sign of total relapse, the client overgeneralizes the single use of a substance as a symptom of total failure, thereby allowing for increasing use over time and in a variety of situations. This is sometimes referred to as the abstinence violation effect (AVE).
2. Selective abstraction—by excessively focusing on the immediate lapse, with an accompanying neglect of all past accomplishments and learning, the client interprets a single slip as equivalent to total failure. The individual measures progress almost exclusively in terms of errors and weaknesses.
3. Excessive responsibility—by attributing the cause of a lapse to personal, internal weaknesses or lack of willpower, the client assumes total responsibility for the slip, which in turn makes reassuming control more difficult than when environmental factors are considered partially responsible for the slip.
4. Assuming temporal causality—here, the client views a slip as the first of many to come, thereby dooming all future attempts at self-control.
5. Self-reference—when the client thinks that a lapse becomes the focus of everyone else's attention, believing that others will attribute blame for the event to the client, this adds to feelings of guilt and shame that may already be present within the person.
6. Catastrophizing—the client believes the worst possible outcome will occur from a single use of the substance instead of thinking about how to cope successfully with the initial lapse.
7. Dichotomous thinking—by viewing events in "black and white," clients view their addictive behavior exclusively in terms of abstinence or relapse and leave no logical room for "gray" areas, where they can get back on track once a slip has occurred.
8. Absolute willpower breakdown—here, the client assumes that once willpower has failed, loss of control is inevitable, never to be regained.
9. Body over mind—the cognitive error here is assuming that once a single lapse has occurred, the physiological process of addiction has exclusive control over subsequent behavior, making continued use inevitable.

These errors in thinking are targeted for change in relapse prevention by helping the client learn how to reattribute the cause of a lapse from internal, stable, personal causes to mistakes or errors in the learning process. To facilitate the client's sense of personal control, lapses are viewed as opportunities for corrective learning, instead of indications of total failure. Congruent with the research in the area (Shiffman, 1991), the therapist presents a lapse as a frequently occurring event in the journey toward recovery. The therapist therefore encourages the client to examine the thoughts and expectancies that surround the lapse closely, with the aim of learning alternative coping skills for similar situations that may arise in the future. By reframing a lapse as a learning opportunity, the client is encouraged to view the event as a chance to hone the skills required for abstinence, thereby countering the cognitive errors of selective abstraction.

To intervene with the errors of overgeneralization and temporal causality, the client is taught to view a lapse as a specific, unique event in time and space, instead of as a symptom with greater significance attached to it (e.g., the beginning of the inevitable end). The errors of self-reference and willpower breakdown can be countered by teaching the client to reattribute a lapse to external, specific, and controllable factors. By examining the difficulty of the high-risk situation, the appropriateness of the coping response employed, and any motivational deficits (fatigue or excessive stress), the client can maintain a sense of control over the event and the process of recovery.

Each of these techniques is aimed at conveying the idea that abstinence is the result of a learning process, requiring an acquisition of skills similar to many other skills one learns. This general metaphor can help the client reverse catastrophizing, by reframing a relapse as a "prolapse," as a fall forward rather than backward. This view, combined with viewing a lapse as a unique event in time, helps the client maintain a sense of personal control, since abstinence or control is framed as just a moment away if use is discontinued.

Several skills are taught to the client in relapse prevention to facilitate these cognitive changes and prevent future lapses. Identifying specific sources of stress that contribute to urges, cravings, or lapses helps isolate the event in time as well as identify other distortions that may be present. For example, clients may identify discussing money with one's spouse as the high-risk situation that preceded a lapse. While discussing the lapse with a therapist, clients can learn to anticipate that discussing money in the marriage may trigger an urge or craving to drink. Teaching clients to use visual imagery, such as viewing the urge as a wave that they can surf, can help manage the feeling that urges will continue to build until they must inevitably be given in to. Self-talk is encouraged if a client believes this will help gain a sense of personal control (such as reciting a phrase to oneself about the goal of abstinence or remembering who can be telephoned when an urge is experienced). In addition, clients are taught to be alert for "apparently irrelevant decisions," which can inadvertently lead to relapse. For example, an abstinent gambler may decide to take a scenic drive through Reno, only to find a situation that would be extremely difficult for many to ignore, thus in this case causing a relapse.

Other theorists have developed treatments based exclusively on changing irrational thinking. Ellis and colleagues (1988) founded a self-help group network called Rational Recovery (RR), based on the principles of rational emotive therapy. Developed as an alternative to the Alcoholics Anonymous network, RR focuses on "addictive thinking" and views abstinence as possible—purely as a result of changing these thought processes. This differs from the relapse prevention model described above, which in its entirety combines cognitive and behavioral techniques. Ellis's RR movement teaches addicts how to identify their own faulty thinking through a self-help manual (Trimpey, 1989) and the attendance at support groups.

See also **Models of Alcoholism and Drug Abuse; Risk Factors for Substance Use, Abuse, and Dependence: An Overview.**

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COGNITIVE-BEHAVIORAL THERAPY

Cognitive-behavioral treatments (CBT) include a group of approaches, grounded in social learning theories of substance abuse (that is, based on classical and operant conditioning, as well as cognitive theory), which emphasize changes in thoughts and behaviors as a means of behavior change. Cognitive-behavioral treatments have been among the most well-defined and rigorously studied psychosocial treatments for substance abuse and dependence. Meta-analysis (Irvin et al., 1999) and reviews of the effectiveness of treatments for substance abuse (APA Workgroup on Substance Use Disorders, 1996; DeRubeis & Crits-Christoph, 1998) have reported that cognitive-behavioral approaches have among the highest level of empirical support for the treatment of substance use disorders and related problems.

OVERVIEW AND STRUCTURE OF CBT

CBT are typically highly structured compared to other approaches used to treat substance use disorders. These treatment approaches are typically comparatively brief (12–24 weeks) and organized closely around well-specified treatment goals. There is typically an articulated agenda for each session and discussion remains focused on issues directly related to substance use. Progress toward treatment goals is monitored closely and frequently, and the therapist takes an active stance throughout treatment.

Cognitive-behavioral approaches typically include a range of skills to foster or maintain abstinence and to prevent relapse, including strategies for issues such as the following:

1. Understanding the individual's patterns of substance use (e.g., factors that precede substance use or change after or during an episode of substance use), sometimes referred to as *functional analysis.*
2. Reducing availability and exposure to the substance and related cues (e.g., people, places, and states that are associated with substance use by its being paired with them during previous episodes of substance use).
3. Fostering the individual's resolution to stop substance use by exploring positive and negative consequences of continued use.
4. Self-monitoring (keeping a diary of activities, craving, and substance use) to identify high-risk situations and to conduct functional analyses of substance use.
5. Recognizing conditioned craving (urges and thoughts about drug use that may be paired with particular cues) and developing strategies to cope with craving.
6. Identifying decisions and thinking styles that can make substance use more likely and learning new strategies to modify those thoughts.
7. Preparing for emergencies and coping with relapse to substance use.
8. Learning substance refusal skills (how to avoid offers of drug and respond assertively).
9. Learning and practicing new behavioral strategies so that the individual can cope more effectively with a range of situations without resorting to substance use or other unhealthy behaviors.

Techniques for teaching these coping responses include direct verbal instruction, modeling appropriate skills through role play, and practice of skills and strategies within the therapy session (Marlatt & Gordon, 1985). Material discussed during sessions is typically supplemented with extra-session tasks (i.e.,

homework) intended to foster practice and mastery of coping skills.

Broad-spectrum cognitive-behavioral approaches such as that described by Monti and colleagues (1989) also include interventions directed to other problems in the individual's life that are seen as functionally related to substance use. These may include general problem-solving skills, assertiveness training, strategies for coping with negative affect, awareness of anger and anger management, coping with criticism, increasing pleasant activities, enhancing social support networks, and job seeking skills.

Various manuals (Monti et al., 1989; Kadden et al., 1992; Carroll, 1998) describe key cognitive-behavioral treatment strategies and techniques, as well as guidelines for their implementation with a variety of types of substance users. The classic resource in this area remains the landmark book by Marlatt and Gordon, *Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors,* which appeared in a second edition in 2005.

The goals of CBT tend to be somewhat broader than those of *strict* behavioral approaches, and the choice of treatment goals dictates the specific interventions implemented with a particular individual. For example, in broad spectrum cognitive-behavioral treatments (e.g., Azrin et al., 1976; Monti et al., 1989), the patient and therapist may select a wide range of target behaviors in addition to a treatment goal of abstinence, including improved social skills or social functioning, reduced psychiatric symptoms, reduced social isolation, and entry into the workforce. Cognitive-behavioral therapy also differs from cognitive therapy through its greater emphasis on building specific behavioral skills (e.g., coping with craving, avoiding high risk situations, understanding behavioral patterns) and somewhat less emphasis on targeting and challenging maladaptive cognitions in the earlier stages of treatment.

STRENGTHS AND WEAKNESSES

Strengths of cognitive-behavioral approaches have been summarized by Rotgers (1996) and include the following:

1. Flexibility in meeting individual needs.
2. Acceptability to a wide range of substance abusing individuals seen in clinical settings.
3. Grounding in established principles of behavior theory and behavior change.
4. Emphasis on linking science to treatment.
5. Well-specified treatment goals and clear guidelines for assessing treatment progress.
6. Emphasis on building self-efficacy.
7. A comparatively strong level of empirical support.

Cognitive-behavioral treatments are highly flexible and can be used in a number of treatment modalities and settings, can be applied across different types of substance use with minor modifications, and are compatible with a wide range of other treatment approaches, including family therapy and pharmacotherapy.

Disadvantages of this group of approaches include the following:

1. Research on these approaches has tended not to emphasize the importance of isolating and evaluating the specific *active ingredients* associated with behavior change.
2. These approaches have tended not to be used much outside academic treatment settings (Rotgers, 1996).
3. Patient motivation and specific procedures for addressing the patient's readiness for change have not been emphasized.

Cognitive-behavioral treatments emerged as a leading approach to the treatment of substance use disorders. Solidly grounded in well-established principles of behavior change, with strong empirical support, and applicable to a wide range of individuals with substance use disorders, these well-defined approaches should be a part of any clinician's treatment repertoire.

See also **Addictive Personality and Psychological Tests; Psychoanalysis.**

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CONTINGENCY MANAGEMENT

Between 1998 and 2008, research progress on contingency management (CM) accelerated substantially, resulting in a sizable literature demonstrating the effectiveness of CM in the treatment of substance use disorders (Higgins, Silverman, & Heil, 2008). CM is effective for increasing abstinence from a variety of drugs of abuse both during and after treatment, increasing compliance with other substance abuse treatment goals, and improving substance abuse treatment outcomes with special populations. After a brief introduction to the theoretical rationale for CM, research in each of these three areas is summarized below.

CM interventions are based on principles of operant conditioning, which is an area of psychology that studies how environmental contingencies of reinforcement and punishment alter the probability of future behavior. There is extensive basic scientific research showing that operant conditioning is involved in important ways in the development of substance use disorders. That is, the drugs that people abuse stimulate the brain's basic reward centers, thereby increasing the likelihood that people will want to take them again, in terms of operant conditioning, an example of positive reinforcement contingency. That is, the consequence of taking the drug is stimulation of the brain reward centers, which increases the likelihood that the person will again take the drug, which produces still further brain reward, and so on. What CM attempts to do is to use similar positive reinforcement contingencies, along with other principles of operant conditioning, to promote therapeutic changes in behavior such as abstaining from drug use, attending therapy sessions, and taking prescribed medications.

The most common use of CM with drug-dependent individuals is to reinforce abstinence from drug use (Lussier et al., 2006; Higgins et al., 2008). Although compelling evidence regarding the efficacy of CM has been available since the 1970s, interest in this treatment approach was bolstered substantially by successes achieved with CM in the treatment of cocaine dependence. In a seminal study on that topic, thirty-eight cocaine-dependent adults were randomly assigned to twenty-four weeks of behavior therapy, including CM, or to drug abuse counseling (Higgins et al., 1993). The CM program used in that study is the model on which many contemporary CM interventions are based. The CM intervention was twelve weeks in duration and explicitly integrated with routine urine toxicology testing. Urine specimens were analyzed at the clinic to minimize delay between obtaining the specimen and delivering appropriate consequences. Cocaine-negative test results earned points that were recorded on vouchers and provided to patients. Points were worth \$0.25 each, with the first negative test results earning 10 points or \$2.50 in purchasing power. To promote sustained abstinence in the outpatient

setting where opportunities to resume drug use are ubiquitous, the number of points earned increased by five with each consecutive cocaine-negative test result, and each three consecutive negative test results earned a $10 bonus voucher. Moreover, a cocaine-positive test result or failure to provide a scheduled specimen reset the value of the vouchers back to the initial low level from which it could escalate again according to the same schedule. Vouchers were often used to purchase retail items such as gym memberships, fishing licenses, or gift certificates to local restaurants. If a patient earned all of the points available across twelve weeks, the individual could earn a total of $997.50 in purchasing power, although average earnings were approximately half of the total possible, which was later determined to be typical in these interventions.

More than 50 percent of patients in the CM condition remained in treatment for the recommended twenty-four weeks and achieved several months of continuous cocaine abstinence whereas only 11 percent of patients in the comparison condition did so. These positive results with CM were particularly encouraging because so few other treatment approaches had been shown to be efficacious with cocaine dependence.

Subsequent studies of CM treatment of cocaine dependence replicated those findings. Studies also have shown that benefits of treatment can persist for almost two years after termination of the CM intervention and that the amount of abstinence achieved during the treatment period is the best predictor of whether the treatment benefits are sustained post-treatment (Higgins et al., 2000; Higgins et al., 2007).

Research has demonstrated effectiveness of CM for increasing abstinence from other drugs of abuse. Also important to note is that reinforcers other than vouchers have been used successfully in CM, such as abstinence-contingent housing employment, take-home medication privileges, and draws from a prize bowl, with the possibility of winning prizes of varying amounts with each draw.

Typically, but not always, CM is used as part of a more comprehensive treatment plan. CM can be used to improve compliance with other treatment goals such as with recommended medication regimens (Rounsaville et al., 2008). Adherence to medications to reduce drug use, such as naltrexone and disulfiram for opioid and alcohol use, can be improved with CM (Carroll et al., 2001). Studies also have demonstrated efficacy of CM in improving medication compliance among tuberculosis-exposed and HIV-infected drug abusers (Elk, 1999). Besides medication compliance, CM can also improve attendance at therapy sessions (Jones et al., 2001) and compliance with participation in therapy-related activities between therapy sessions (Bickel et al., 1997; Iguchi et al., 1997). In these latter applications, patients earn vouchers by completing some minimum number of therapy-related activities weekly. The activities might include attending a job interview if the goal was gaining employment or attending a self-help meeting if the goal was to increase contact with a social network to support sobriety. Vouchers are provided when patients submit documentation verifying that they had completed a designated therapeutic activity. Completion of therapeutic activities is associated with greater drug abstinence.

CM also is capable of improving outcomes with important special populations of drug abusers. For example, effective treatments are sorely needed for drug-dependent pregnant women. A voucher-based CM intervention has been demonstrated to significantly increase abstinence from cocaine and heroin use while simultaneously increasing vocational skills among pregnant women who were both drug dependent and chronically unemployed (Silverman et al., 2002). Vouchers delivered contingent on abstinence from cigarette smoking increased cessation rates during pregnancy and postpartum (Donatelle et al., 2000; Higgins et al., 2004) and increased fetal growth (Heil et al., in press). Other special populations for whom CM interventions show promise are adolescents (Kamon et al., 2005; Krishnan-Sarin et al., 2006), the homeless (Milby et al., 2000), and people with serious mental illness (Roll et al., 2004).

Sufficient research has been conducted to glean some rules about effective implementation of CM. Below are ten features of effective CM interventions:

1. The details of the intervention must be explained carefully to patients prior to beginning treatment, with written contracts being very helpful.

2. The response being targeted by the CM intervention (e.g., drug abstinence) should be defined in objective terms (e.g., drug-negative urine toxicology results).
3. The objective methods to be used for verifying that the target response occurred (e.g., urine toxicology testing) should be identified in advance.
4. The schedule for monitoring progress (e.g., Monday, Wednesday, & Friday) should be outlined clearly.
5. The schedule for monitoring progress should include frequent opportunities for patients to experience the programmed consequences.
6. The duration of the intervention should be clearly stipulated in advance.
7. Focusing on a single target (e.g., abstinence from a single substance) on average produces larger treatment effects than those that target multiple targets (e.g., abstinence from multiple substances).
8. The consequences that will follow success and failure have to be clear.
9. There should be minimal delay in delivering designated consequences. Delivering the consequence on the same day that the target response is verified produces larger treatment effects than delivering the consequence at a later time.
10. Larger value incentives on average produce larger treatment effects.

CM is effective in increasing drug abstinence and in improving compliance with treatment regimens for various types of drug dependence and populations. Positive outcomes have been achieved even with some of the most challenging and recalcitrant subgroups of drug abusers. Though there is a loss of treatment gains when the intervention is terminated, beneficial carryover effects have been demonstrated for a year or more post-treatment and the rates of relapse appear to be comparable to other interventions. Nevertheless, prevention of relapse is an important problem needing improved methods to manage it. Systematic use of multimodal interventions designed to address the many changes likely to be necessary for longer-term success is one reasonable approach, as is the development of longer-term CM interventions that can be kept in place until the patient gains the requisite skills to sustain abstinence without CM support.

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COUPLES AND FAMILY THERAPY

Since the late 1970s, there has been growing recognition that relationship factors between couples and among families play a crucial role in maintaining substance abuse. Substance misuse and relationship problems have a reciprocal relationship where each exacerbates problems in the other, producing a vicious cycle that is difficult to escape.

Among couples, ineffective problem-solving, poor communication, conflict, financial strain, and nagging are common antecedents to substance use and abuse. Caretaking by the non-substance-abusing spouse following drinking or drug use can inadvertently reinforce substance use. Additionally, spouses' resentments, while understandable, can lead to ignoring rather than reinforcing abstinence.

BEHAVIORAL COUPLES THERAPY TREATMENT

Behavioral couples therapy (BCT) was founded upon two fundamental assumptions. First, family members can reward abstinence. Second, relationship distress and conflict are powerful antecedents to substance use, and reduction of these antecedents improves treatment outcomes. The following is an overview of some of the defining approaches used in behavioral couples therapy (see O'Farrell and Fals-Stewart [2006] for more details).

Supporting Abstinence with Recovery Contract. In early treatment phases, the therapist and the couple collaboratively develop a Recovery Contract, consisting of a daily Trust Discussion in which the substance-abusing partner expresses the intention to refrain from alcohol or drugs, and the non-substance-abusing partner verbally supports the patient's efforts. For patients medically cleared and willing, daily use of medications supporting sobriety (i.e., disulfiram, naltrexone) is witnessed and verbally supported by the spouse. Completion of Recovery Contract components, including the Trust Discussion, medication adherence, and additional

components (e.g., Alcoholics Anonymous, Al-Anon attendance) are recorded daily on a calendar provided by the therapist. Both partners agree to limit discussions of past substance use to the therapy session where communication can be monitored and mediated as necessary to reduce substance-related conflicts, which may trigger relapse.

Improving Couple Relationship Functioning. Through standard couple-based behavioral assignments, BCT aims to increase positive feelings, shared activities, and constructive communication. Exercises include noticing and acknowledging pleasing behaviors performed by one's partner daily, planning ahead to surprise the partner through activities that demonstrate caring, and engaging in rewarding shared activities. Additionally, communication skills training (e.g., paraphrasing, empathizing, validating) can help the couple better address stressors as they arise, reducing the risk of relapse.

Relapse Prevention and Maintenance. The final stages of BCT involve relapse prevention including ongoing sobriety-related activities (e.g., daily Trust Discussion, self-help support meetings) and contingency plans for relapses (e.g., contacting the therapist and a sponsor).

EMPIRICAL BASIS FOR BCT

Multiple studies indicate that participation in BCT (O'Farrell & Fals-Stewart, 2006) is associated with positive outcomes for alcoholic and drug-abusing patients. BCT produced better outcomes than more typical individual-based treatment for married or cohabiting alcoholic and drug-abusing patients in a meta-analysis of 12 controlled studies (Powers et al., 2008), some of which are summarized below, and details are provided in O'Farrell and Fals-Stewart (2003, 2006).

Primary Clinical Outcomes. Fourteen studies comparing substance use and relationship outcomes for primarily male, substance-abusing patients show a fairly consistent pattern of greater rates of abstinence and fewer substance-related problems, happier relationships, and lower risk of divorce and separation among those who receive BCT than patients who receive individual-based treatment.

Benefit-to-Cost Ratio. Three BCT studies (two in alcoholism and one in drug abuse) examined social costs due to substance abuse and found savings that averaged $5,000–$6,500 per case, with every dollar spent delivering BCT saving five dollars in social costs. BCT was more cost effective than individual treatment for drug abuse or interactional couples therapy for alcoholism.

Domestic Violence Outcomes. Two studies with male alcoholics found male-to-female violence was significantly reduced after BCT and nearly eliminated with abstinence. Two studies showed that BCT reduced partner violence and couple conflicts better than individual treatment.

Impact of BCT on Children. Two studies (one in alcoholism, one in drug abuse) demonstrated greater improvements in functioning among children when parents received BCT for substance abuse than among children when parents received individual-based treatment or couple psychoeducation. Significant reductions in the number of impaired children were found only for those receiving BCT.

Integrating Recovery-related Medication. Among male opioid patients taking naltrexone, BCT patients had better naltrexone compliance, greater abstinence, and fewer substance-related problems than those in individual treatment. BCT also resulted in improved compliance with HIV medications and with disulfiram and naltrexone for alcoholic patients.

BCT with Other Family Members. While most BCT studies involve traditional couples, some recent studies, including those described above, successfully expanded the use of BCT to include family members beyond spouses. For example, in the studies of BCT with HIV medications among drug abusers and naltrexone use for opioid patients, family members included heterosexual partners, homosexual partners, parents, siblings, and roommates. The outcomes for nonspousal dyads resulted in as much success as those for spousal dyads. Specifically, Fals-Stewart and O'Farrell (2003) found no significant differences across outcome measures between the spousal and nonspousal dyads for opioid patients.

CONTRAINDICATIONS FOR BCT

Contraindications to consider in the use of BCT include current psychosis for either member of the couple, acute risk of severe family violence, or an active court order requiring the couple to have no contact. Cases with less severe forms of family violence can be treated successfully in BCT with conflict containment as an explicit goal from the outset and with specific steps taken to avoid violence (for more details see O'Farrell & Murphy, 2002). Finally, if both members of the couple have a current substance use problem, BCT may not be effective; possible exceptions to this are when one member has at least 90 days of abstinence or both members decide to change their substance use within the first few treatment sessions.

Future Directions for BCT. Research is needed to replicate and extend recent advances, particularly for women and broader family constellations. There is a great need for research on BCT for dual-using couples, as this difficult clinical challenge has yet to be addressed empirically. Finally, there is a need for technology transfer so that additional families can benefit from existing knowledge about the effectiveness of BCT for alcoholism and drug abuse.

See also **Al-Anon; Alcoholics Anonymous (AA); Families and Drug Use; Intimate Partner Violence and Alcohol/Substance Use; Naltrexone; Opiates/Opioids; Treatment, Pharmacological Approaches to: Disulfiram; Treatment, Pharmacological Approaches to: Naltrexone.**

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GROUP THERAPY

Group therapy is the most common treatment modality for substance use disorders (SUDs). Broadly defined, group therapy for SUDs consists of two or more unrelated patients and a therapist who meet together regularly, with the primary goal of reducing or eliminating substance use or addressing behaviors related to substance use.

A 1988 study indicated that 94 percent of SUD treatment facilities in the United States offered group therapy of some type (Price et al., 1991). It is unlikely that this figure has decreased since that time, given the increased emphasis on reducing costs in such facilities. Group therapy is a popular choice for patients with SUDs because of its perceived cost-effectiveness, and because of the powerful influence of self-help (also called mutual-help) groups such as Alcoholics Anonymous (AA), Narcotics Anonymous (NA), and SMART Recovery. A key idea behind these groups is that the influence of group members with similar experiences can help to reduce the denial frequently associated with substance use. Other central ideas behind self-help groups are the beliefs that members can benefit from: (1) developing supportive interpersonal relationships with others, (2) recognizing and expressing needs and emotions, and (3) identifying and changing maladaptive patterns of behavior. It is likely that nearly all forms of group therapy share these benefits to varying degrees.

TYPES OF GROUP THERAPY

There are five basic models of group therapy:

1. the group education model, in which the group leader serves as a teacher and instructs patients about the effects of drug and alcohol use on the brain and body as well as the natural course of addiction and recovery.

2. recovery skills training (also educationally based), which has the aim of teaching specific behavioral and cognitive-behavioral skills. These include recognizing, avoiding, and coping with triggers to substance use; drug-refusal skills; problem solving; and cognitive restructuring.
3. the group process model, in which the therapeutic effect is related to the nature of the interaction (either supportive or confrontational), both among group members themselves and between group members and the group leader. These groups emphasize the parallels between such interactions and relationships outside of the group therapy setting.
4. the check-in group, which essentially consists of brief individual treatment, including goal-setting and a review of progress toward goals, conducted in a group format.
5. group treatment that addresses other issues that are relevant to substance use, including anger management, communication, assertiveness, relaxation, or parenting skills.

EFFECTIVENESS

A review of 30 studies examining the effectiveness of group therapy for SUDs revealed three primary findings. First, the results of several studies suggest that group therapy is generally more effective than no treatment, and that group therapy can increase the effectiveness of existing treatments. This finding may be reassuring to those who may fundamentally question whether group therapy is helpful at all.

Second, no specific type of group therapy has been found to be generally most effective at improving SUD outcomes. However, several promising interventions have shown at least some evidence of being more effective than others, usually in treating specific populations. For example, there is evidence that integrated group therapy is superior to group drug counseling in reducing substance use in patients diagnosed with both bipolar disorder and SUD (Weiss et al., 2007). Preliminary data also indicate promise for women's recovery groups when compared to mixed-gender group drug counseling in treating women with a SUD (Greenfield et al., 2007). Solution-focused group therapy has demonstrated superior results to problem-focused group therapy in reducing substance use in people identified as having a substance abuse problem that requires less than nine hours per week of treatment (Smock et al., 2008). Similarly, a family systems intervention for adolescents yielded superior substance use outcomes when compared to either group drug education or a process-oriented group therapy (Joanning et al., 1992).

There have also been promising results for a substance abuse-domestic violence group treatment compared to a twelve-step facilitation group for men exhibiting domestic violence and SUD (Easton et al., 2008). Multidimensional family therapy has demonstrated superior outcomes to peer group therapy in measures of substance use and behavioral problems with low-income, ethnically diverse young adolescents (Liddle et al., 2007). Finally, a behavioral skills intervention was superior in effectiveness to transactional analyses in treating adult males with an alcohol use disorder (Olson et al., 1981).

The third finding is that there is no evidence that group therapy is superior to individual therapy, or that individual therapy is superior to group therapy, when the content, intensity, and length of treatment are equivalent. This is an important finding for the proponents of group therapy, given its presumed cost-effectiveness and its widespread inclusion in SUD treatment throughout the country. Conversely, it also supports the idea that group therapy is not intrinsically superior to individual approaches.

However, a failure to find differences between treatments does not necessarily mean that the treatments compared are equally effective. These outcomes may have arisen from several factors, all of which can influence statistical power, or the ability to detect a difference when it exists. The size of the measured treatment effect is one determinant of statistical power, which is in turn influenced by the treatment intensity and duration. Statistical power is also influenced by the number of participants in a study, as well as by variations in how treatment is delivered.

Perhaps the most important finding in examining the treatment literature on group therapy is that so few studies of this treatment modality have been conducted. Given how frequently group therapy is used to treat SUDs, this is particularly noteworthy. Between 1978 and 2008, there were only 30

published papers from prospective treatment studies comparing group therapy to other treatments. Unfortunately, with the few exceptions noted earlier, it is difficult to establish firm conclusions about what frequency, duration, or type of group treatment is most effective with particular populations. Despite the widespread clinical acceptance of group therapy for SUDs, relatively little is really known about its effectiveness. The outcome studies on this topic are limited in number, and the findings are generally mixed.

See also **Families and Drug Use; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Sobriety; Toughlove.**

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LONG-TERM VERSUS BRIEF

For many people, alcohol and drug abuse has the characteristics of chronic disorders, such that people experience recurring cycles of cessation and relapse (Hser, Anglin, Grella, Longshore, & Prendergast, 1997). Therefore, researchers and practitioners have increasingly accepted the idea that substance dependence is a chronic disorder (Donovan, 1998; McLellan, 2002). Like substance use disorders (SUDs), many medical and psychiatric disorders have a chronic course. With such disorders, longer-term treatments are usually found to be much more effective than short interventions. For example, most patients with disorders such as hypertension, elevated cholesterol, diabetes, or schizophrenia have the best clinical course if they maintain lifestyle modifications and remain on their medications for extended periods of time. One would therefore think that individuals with SUDs who seek treatment would have better outcomes if they received longer, as opposed to shorter, episodes of care. However, research findings in the addictions have indicated that the relationship between length of treatment and outcome is not particularly straightforward.

There is considerable evidence that patients who stay in treatment longer have better outcomes (Simpson, 2004). That is, when patients with similar demographic characteristics and pretreatment substance use severity all enter the same treatment program, those who stay in treatment longer will, on average, have better treatment outcomes that those who leave early. However, it is not clear how much the better outcomes should be attributed to longer stays in treatment or to individual characteristics such as motivation and initial success in treatment. The most

direct way to untangle treatment from motivation effects and other patient characteristics is to conduct studies in which patients are randomly assigned to the same or similar treatments of different lengths, and their outcomes examined over time. Studies of this sort have produced very little evidence to indicate that treatments with longer durations produce better substance-abuse outcomes than those with shorter durations (Miller & Hester, 1986; McCusker et al., 1995; Kamara & Van Der Hyde, 1997; Long, Williams, & Hollin, 1998; Trent, 1998; Stephens, Roffman, & Curtin, 2000). One potential factor contributing to this result is that treatments in these studies are relatively short, such that the long conditions seldom exceed 90 days. Hence, these studies have not directly examined if extended interventions generate better outcomes than standard-length (i.e., 90-day) treatments (McKay, 2005).

In addition, it should also be stressed that many substance-abuse treatment programs feature a continuum of care, in which patients spend a certain amount of time in an initial higher-intensity treatment and then "step down" to a lower-intensity level of care, such as aftercare. Would participation in and completion of aftercare following initial treatment have greater prognostic significance than the duration of a single level of care? Earlier research suggested that such was not the case (McKay, 2001). In the majority of the relatively few studies that examined this issue, patients who were randomly assigned to active aftercare treatments did not have better substance use outcomes than those who were randomized to either no aftercare or minimal aftercare conditions. In a more recent study that examined new continuing care approaches, McKay (2006) summarized the key findings:

> 1) Continuing care interventions of a year or longer are more likely to show significant positive effects; 2) continuing care treatments that are less burdensome to patients appear to promote higher rates of sustained engagement; 3) more structured and intensive continuing care may be more effective for patients with severe substance dependence and associated problems and for those who fail to achieve reasonable progress while in the initial phase of treatment; and 4) use of medications as part of continuing care is increasing. (p. 355)

In a recent review of extended interventions (i.e., therapeutic protocols that have a planned duration of longer than 6 months) for alcohol and drug use disorders, McKay (2005) examined interventions in two categories: (1) Interventions contained either behavioral or pharmacological treatments, which were provided over periods of greater than 6 months. These interventions consisted of face-to-face contact with counselors or therapists and were provided primarily in clinics and other treatment facilities. This category included some studies reviewed by McKay in 2001. (2) Lower-intensity interventions involved the regular monitoring of patients' symptoms and status throughout extended periods of time. Monitoring was conducted through face-to-face contacts with research or treatment personnel or through telephone contacts using an interactive voice response system. In some of these monitoring protocols, patients were linked to services or were provided with brief counseling when their conditions warranted additional support.

The results of this comprehensive review indicated that maintaining therapeutic contact with individuals with SUDs for extended periods of time seemed to promote better long-term outcomes than "treatment as usual." Although most of the extended behavioral and pharmacological interventions reviewed in this article yielded positive effects, two studies did not (Prendergast, Hall, Wexler, Melnick, & Cao, 2004; Krystal, Cramer, Krol, & Kirk, 2001) and several other studies with various methodological limitations produced mixed results (Braukmann et al., 1985; Dahlgren & Willander, 1989; Ojehagen et al., 1992; Tomson, Romelsjo, & Aberg, 1998; McCrady, Epstein, & Kahler, 2004). In addition, McKay pointed out an important issue regarding study design: "In many studies the extended interventions were compared to relatively low intensity or placebo control conditions rather than to shorter versions of the same intervention, which raises questions about how 'extended' an extended intervention needs to be for effective addiction management" (2005, p. 1603). Therefore, before any firm conclusions can be drawn about the utility of extended treatment in the addictions, future research that directly compares extended behavioral and pharmacological interventions to treatment as usual or shorter versions of the same interventions is needed (McKay, 2005).

Overall, consensus exists among clinicians and clinical researchers that sustained recoveries from

SUDs generally require ongoing efforts by those who have these disorders. Some of the behaviors associated with good long-term outcomes include regular attendance of self-help groups such as Alcoholics Anonymous, treatment for family or marital problems, employment, involvement with a religious group, and a commitment to new interests or hobbies. These findings are consistent with the notion that formal treatment, whether of short or long duration, is useful to begin a process of change that must be sustained over long periods of time to be successful and that ultimately involves many areas of functioning.

See also **Diagnosis of Substance Use Disorders: Diagnostic Criteria; Research: Motivation.**

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MINNESOTA MODEL

Origins of the Minnesota Model of alcohol and drug abuse treatment are found in three independent Minnesota treatment programs: Pioneer House in 1948, Hazelden in 1949, and Wilmar State Hospital in 1950. The Hazelden Clinics remain in existence as of 2008 and are located in Minnesota, New York, Illinois, Oregon, and Florida. The original treatment programs recognized Alcoholics Anonymous (AA) as having success in bringing about recovery from alcoholism. Unique to this early stage of the Minnesota Model was the blending of professional behavioral science understandings with AA's principles. Important in the development of the Minnesota Model is the way treatment procedures emerged, from trial and error, from acknowledgment of the mutual help approach of AA, and from the use of elementary clinical assumptions rather than a well-developed theoretical position. In many ways, the Minnesota Model developed from a grassroots, pragmatic movement.

ASSUMPTIONS OF MINNESOTA MODEL

Because of its noncentralized development, the Minnesota Model is not a standardized set of procedures but an approach organized around a shared set of assumptions. They were articulated by Dan Anderson, the former president of Hazelden Foundation and one of the early professionals working with the Minnesota Model at Wilmar State Hospital. The assumptions indicate that alcoholism is (1) a cluster of symptoms; (2) an illness characterized by an inability to determine time, frequency, or quantity of consumption; (3) non-volitional (alcoholics should not be blamed for their inability to drink alcohol moderately); (4) a physical, psychological, social, and spiritual illness; and (5) a chronic primary illness, meaning that once manifest, a return to non-problem drinking is not possible. Although these assumptions are phrased as pertaining to alcoholism, early experience with the Minnesota Model demonstrated that drug addiction can also be understood and treated within these assumptions. *Chemical dependency* is the term generally used by clients and treatment providers when referring to substance use disorders in this model. The Minnesota Model provides treatment for chemical dependency for both alcohol and other drugs.

A twenty-four- to twenty-eight-day inpatient treatment stay, or approximately eighty-five hours in outpatient rehabilitation, characterizes Minnesota Model treatment. Inpatient treatment may occur in hospital settings or free-standing facilities and may be run by for-profit or nonprofit organizations. Different treatment settings have different mixes of staff positions, but the multidisciplinary team of medical and psychological professionals plus clergy and counselors are frequently found, either in a close interacting network or a more diffuse working arrangement.

Primary counselors have either received specific training in the Minnesota Model approach to treatment or have learned their counseling skills in an apprentice-like placement. Most counselors are not mental-health-degreed professionals or holders of medically related degrees, but they are commonly working on their own twelve-step programs because of life experience with chemical dependency or other addictions. As in AA, this shared personal experience of both clients and counselors is important for the client/counselor relationship and the modeling the counselor provides for the client.

Minnesota Model treatment programs vary in the centrality of counseling staff and the programmed autonomy of the treatment experience. Some treatment programs have the counselor facilitating the majority of the groups and actively directing the treatment experience. Other programs have the group members carrying out the treatment experience while the counseling staff maintains a low profile as they seek to empower clients to acquire the insights and resources necessary for their recovery. Treatment also varies in the amount of confrontation employed, the presence of a family program requirement (which is central with adolescents), the extent of assigned reading, the detail of client record documentation, and other attributes.

Minnesota Model treatment is without exception characterized by the use of AA principles and understandings (steps and traditions) at the core of

the treatment experience. Clients are provided with the *AA Big Book* (Alcoholics Anonymous) and *The Twelve Steps and Twelve Traditions*. Both of these books are required reading. Spirituality is emphasized as important to recovery, which is consistent with the AA understanding. AA group meetings occur in the schedule of rehabilitation activities, and clients may visit a community AA meeting as part of their treatment experience. Clients work on AA steps during their treatment experience; some programs focus on the first five steps whereas others emphasize all twelve steps.

Treatment is not just an intensive exposure to AA. It motivates treatment participants to develop mutual trust and to share and be open about how the use of substances has come to control their lives. Clients are told that they have a chronic disorder. Their behavior has been directed by the disorder, but they have been unable to see the consequences of their behavior because the disorder can give rise to denial.

Treatment plans are individualized based on assessments by the multidisciplinary staff. Generally, the first goal of treatment is to break the client's denial, and the second goal is for the client to accept the disease concept. Because treatment has clients ranging from new admissions to those ready to complete their program, senior peers are influential in helping clients who are in the early stages of treatment to understand denial and the disease concept.

The message in the final treatment stage is acceptance and awareness that individuals are able to change if they take appropriate action to deal with a chronic condition. The rehabilitation staff develops an aftercare plan with clients that will continue to support some of the changes that have taken place during treatment and to encourage changes that will promote ongoing recovery. Characteristically, clients comment on their increased awareness of the simple pleasures of life. They are told that they must continue to work the AA steps, attend AA meetings, and address other problems of living if they are going to experience recovery. It is emphasized that primary treatment is just one part of an ongoing continuum of care. Recovery is hard work made even more difficult by possible bouts of craving to drink or use drugs, by periods of depression, problems of regaining trust from their family, and establishing new friends and activities not tied to alcohol and drug use.

There have been few published reports of the effectiveness of Minnesota Model treatment programs. These include outcome studies prepared by Hazelden for treatment programs in the Hazelden Evaluation Consortium and peer-reviewed publications. This body of work generally indicates that for clients treated with the Minnesota Model, about 50 percent of those treated, including non-completers, are abstinent for one year following discharge from treatment. This percentage is higher for treatment completers and for clients having fewer complications and more stability in their lives. About one-third of the clients return to heavy use patterns within the year, and the remainder has slips or a period of resumed drinking/use but also sustained periods of abstinence. Abstinent clients have fewer legal, health, interpersonal, and job-related problems, and about 75 percent attend AA and/or continuing care.

The Minnesota Model is a label applied to a broad range of programming that is primarily based in the principles of AA. While its suitability for all addicts merits further study, this approach represents a highly visible treatment modality serving a large number of clients, including adolescents, throughout the United States. It has a counterpart known as the Icelandic Model, and both of these treatment models have significantly influenced treatment in Sweden and other parts of Scandinavia. International interest in adopting the Minnesota Model appears to be growing, with scattered treatment programs appearing in many countries. Little research has been done as of 2008 on the transportability of this treatment model to other cultures.

See also **Treatment: An Overview of Alcohol Abuse/Dependence; Treatment: A History of Treatment in the United States.**

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MOTIVATIONAL AND BRIEF

Brief interventions can be used as preventive interventions for individuals at risk of developing an alcohol or drug use disorder or as treatment for those meeting the diagnostic criteria of the American Psychiatric Association (APA) for a substance use disorder (SUD). These interventions, which can be delivered one-on-one or in a group setting, can often increase an individual's readiness to change his or her substance use behavior and motivate that individual to enter longer-term treatment. Although facilitators can deliver brief interventions using a variety of styles, the discussion here will focus on brief interventions that utilize a motivational interviewing style.

Motivational interviewing, devised by Drs. William Miller and Stephen Rollnick, is a nonjudgmental and nonconfrontational counseling style. It emphasizes client-centeredness and uses a direct but collaborative approach to help clients explore and resolve their ambivalence about changing their substance use. Facilitators elicit behavior change from the client's own resources instead of imposing their views on the client. In contrast to an expert or authoritarian role that confronts, educates, and convinces clients to change, facilitators using motivational interviewing assume a partnership role with clients and respect a client's autonomy and freedom to change.

Motivational interviewing techniques overlap with other forms of therapy and have been captured in the acronym OARS. Facilitators ask or make *open-ended* questions and statements (e.g., "Tell me more about your drinking"), praise and sincerely *affirm* the client (e.g., "I appreciate you taking the time to come in today"), *reflect* back to the client what he or she has expressed (e.g., "From what I hear you saying, you have been worried about your health for quite a while"), and *summarize* periodically and at the end of the session (e.g., "You like drinking because you feel it helps you relax, improves your mood, and makes it easier to talk with people in social situations"). The facilitator selectively uses OARS to elicit client "change talk" or language related to the client's desire, ability, reason, and need to change.

Brief interventions that utilize motivational interviewing typically range between one and four sessions and vary in the amount of structure. As an unstructured preventive intervention, the facilitator and client discuss a client's substance use in an open-ended manner (i.e., without a manual to follow). As a structured treatment, the facilitator uses a manual or guide and discusses specific components of the intervention (e.g., normative feedback and drinking expectancies). Motivational enhancement therapy, developed by Miller and colleagues, is an example of a four-session manualized brief intervention for Project MATCH (Matching Alcoholism Treatments to Client Heterogeneity). The key components of motivational enhancement therapy are described in the acronym FRAMES: Facilitators provide *feedback* to an individual about the costs and consequences of alcohol and drug use (e.g., "Compared to other women your age, you drink at the 75th percentile"), encourage *responsibility* for the change to come from the client rather than the facilitator (e.g., "This information is just for you, it's up to you what you'd like to do with it"), give *advice* to change as part of talking about change and setting goals (e.g., "You've discussed several methods of drinking less to improve your health. If it's okay with you, I'd also recommend that you make an appointment with your physician to have your liver evaluated"), offer clients a *menu* of alternative self-help or treatment options, use an *empathetic* style, and enhance the client's *self-efficacy* (e.g., client's belief that he or she has the ability to change). Brief interventions vary in the amount of structure when used as a preventive intervention or treatment.

EFFECTIVENESS OF BRIEF INTERVENTIONS AND MOTIVATIONAL INTERVIEWING

Research suggests that brief interventions are effective in reducing substance use and related consequences and facilitating treatment entry and aftercare. Brief interventions are most effective for individuals with at-risk drinking and drug-related problems that have not yet developed into alcohol or drug dependence. In these studies, heavy use and substance-related consequences tend to improve. However, studies such as Project MATCH have shown that brief interventions can be helpful for individuals with alcohol dependence. In Project MATCH, individuals who received motivational enhancement therapy showed treatment outcomes (e.g., abstinence from alcohol one and three years after treatment) similar to those of individuals who received twelve-session cognitive-behavioral therapy (CBT) or twelve-step facilitation therapy. Although brief interventions are often associated with positive lifestyle improvements and a decrease in negative consequences from substance use, these effects tend to diminish over time. Brief interventions have also been shown to enhance treatment entry, program attendance, treatment adherence, and aftercare compliance for substance use. Thus, they can help to engage clients at multiple levels of treatment.

The flexibility of brief interventions allows them to be delivered by facilitators of diverse backgrounds and in diverse settings. For example, research suggests that brief interventions can effectively be delivered by facilitators who do not specialize in addiction treatment. With the proper training and supervision, brief interventions that utilize a motivational interviewing style can be equally effective when delivered by therapists, physicians, social workers, nurses, or peers. Brief interventions are also efficacious in a variety of settings, including medical settings (e.g., during routine visits as part of primary care, prenatal care, or other hospital stays), emergency departments (e.g., when individuals are being treated for alcohol- or drug-related consequences in emergency rooms and trauma centers), and other nonmedical settings (e.g., the criminal justice system, police stations, college settings, or employee assistance programs). These interventions may also be used with both adults and adolescents. Adolescents receiving a brief intervention tend to have decreased substance use, fewer negative consequences, and increased treatment adherence. In summary, research supports the use of brief interventions across a variety of settings that can be delivered by diverse facilitators and utilized by adults and adolescents alike.

Additional research is needed in the area of brief motivational interviewing interventions that examine outcomes with different populations (e.g., different racial or ethnic groups, different age groups, and other addictive behaviors), investigate methods of sustaining longer-term outcomes, and compare the effectiveness of different components of brief interventions (e.g., frames and in-person versus phone delivery). Brief interventions and motivational interviewing are an innovative and cost-effective approach to addressing alcohol and drug problems.

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SELF–HELP AND ANONYMOUS GROUPS

The recovery process does not end when an individual completes a drug rehabilitation program. Due to the relapsing nature of substance abuse, individuals receiving treatment for the disorder are generally urged to participate in some form of continuing care after their initial phase of treatment has ended

(McKay et al., 2004). Self-help (also known as mutual aid) support groups play a vital role: The great strain on health care resources has led the treatment system to become increasingly reliant on these groups as complements or alternatives to professional treatment (Atkins & Hawdon, 2007).

TWELVE-STEP MODEL

Support groups using the twelve-step model are the most widely known and play a major role in the treatment protocols of many treatment facilities. The original twelve-step program, Alcoholics Anonymous (AA), is the most widely used treatment in the United States for those with alcohol problems. Similar groups include Narcotics Anonymous, Cocaine Anonymous, Emotions Anonymous, Gamblers Anonymous, and others. The twelve steps were devised in the late 1930s by William Griffith Wilson (1895–1971), known as Bill W., a major cofounder of AA, in conjunction with a small group of his early followers. The Twelve Steps of Alcoholics Anonymous (Alcoholics Anonymous, 2001) are as follows:

1. We admitted we were powerless over alcohol—that our lives had become unmanageable.
2. Came to believe that a Power greater than ourselves could restore us to sanity.
3. Made a decision to turn our will and our lives over to the care of God as we understood Him.
4. Made a searching and fearless moral inventory of ourselves.
5. Admitted to God, to ourselves, and to another human being the exact nature of our wrongs.
6. Were entirely ready to have God remove all these defects of character.
7. Humbly asked Him to remove our shortcomings.
8. Made a list of all persons we had harmed, and became willing to make amends to them all.
9. Made direct amends to such people wherever possible, except when to do so would injure them or others.
10. Continued to take personal inventory, and when we were wrong, promptly admitted it.
11. Sought through prayer and meditation to improve our conscious contact with God as we understood Him, praying only for knowledge of His will for us and the power to carry that out.
12. Having had a spiritual awakening as the result of these steps, we tried to carry this message to others, and to practice these principles in all our affairs.

Twelve-step programs offer an informal treatment adjunct to professional care, using a support community of peer volunteers. There are no dues or fees for AA membership, and the only requirement for membership is a desire to stop drinking. The AA organization focuses exclusively on helping individuals recover from alcoholism, and as a matter of policy has no opinions on outside issues of any kind. It is fully self-supporting and declines outside contributions, with the intention of minimizing distraction, controversy, and disunity (Kelly, 2003).

Related groups include Al-Anon, a group dedicated to helping the friends and relatives of alcoholics, and Ala-teen, which is aimed at teenagers who have a family member or friend who is alcoholic.

Although AA does not affiliate with outside facilities, in the 1950s its philosophy was borrowed by and incorporated into professional drug treatment programs in the United States. This influential approach, dubbed the *Minnesota Model*, uses a treatment package encompassing abstinence, behavior change, and attending AA meetings. A 1998 study found that 90 percent of private substance use disorder treatment centers in the United States based their treatment on the twelve-step model (Kelly, 2003).

CONTROVERSY OVER AA

Despite its popularity, AA remains one of the more controversial and least understood and assessed approaches to alcoholism treatment (Morgenstern et al., 1997). Some have argued that it is difficult to assess the independent effects of self-help groups, due to their integration with professional treatment. Research shows a high sobriety rate for alcoholics strongly devoted to the AA program, but adherence is a problem: Those who attend frequently and actively participate seem to benefit but the dropout rate is high.

Spiritual Component. The twelve-step approach has a strong spiritual component, as treatment recovery steps include admitting powerlessness over the addiction and surrendering to a "higher power." This powerlessness is seen as a lifetime condition, and the twelve steps are seen as providing a

mechanism for ensuring a lifetime cessation of the compulsive behavior. Some argue that non-religious individuals might be turned off by the perceived spiritual or religious emphasis. Others suggest that a moderation approach works better than abstinence-only with some individuals. These different opinions have led to increased interest in answering the question: For whom are twelve-step meetings particularly helpful or not helpful?

In the early twenty-first century, some members of AA have made an effort to separate AA from its original quasi-religious roots. For example, Griffin (2004) writes that a Higher Power can be interpreted as God, or as a non-monotheistic object, including the AA group itself. This movement may help improve AA attendance among atheists and agnostics, as these individuals were less likely to initiate and sustain AA attendance compared to those who identify themselves as religious. Interestingly, belief in God prior to AA attendance did not provide any advantage in obtaining AA-related benefits (Tonigan, 2007).

ALTERNATIVE VERSIONS OF TWELVE-STEP PROGRAMS

Studies have revealed that substance use disorders frequently co-occur with psychiatric illnesses such as depression, anxiety, or personality disorders. To address the needs of this population, self-help groups specifically designed for dual diagnosis patients have emerged, such as Double Trouble in Recovery and Dual Recovery Anonymous. These groups follow a modified twelve-step approach, incorporating specific components for addressing the mental health needs of the participants. For example, participating in Double Trouble in Recovery meetings has been associated with better medication compliance, which may be particularly helpful for individuals with serious mental illnesses, such as schizophrenia and bipolar disorder that also have a high rate of co-occurring substance abuse.

While twelve-step groups dominate treatment centers, there are also a number of important mutual-aid support groups using alternative approaches to recovery. In contrast to the acceptance of a "Higher Power," Secular Organizations for Sobriety (SOS) groups emphasize a secular approach, using cognitive tools to support recovery. Founded in 1985, SOS emphasizes personal responsibility and self-reliance in its abstinence-based program. Participants commit to a lifelong Sobriety Priority, agreeing to abstain from all drugs or alcohol. SOS does have a suggested meeting format, but each meeting is autonomous, and formats vary considerably, reflecting the desires of the individual group. For example, the largest chapter of SOS (centered in northern California) changed its name to LifeRing Secular Recovery in 1999 but remains integrated within SOS as a whole.

Women for Sobriety. Another alternative to the twelve steps is Women for Sobriety (WFS). Founded in 1976, WFS rests on the belief that women have different needs than men in recovery. WFS groups are run by a certified moderator in a conversation format and generally take place at least once per week. The New Life Program provides structure to the meetings, including a statement of purpose, weekly topic guide, and other literature. WFS seeks to develop in female alcoholics a strong feeling of self-worth while acknowledging that they have symptoms of a serious disease.

Rational Recovery and SMART Recovery. In 1988, licensed social worker Jack Trimpey founded Rational Recovery (RR), an organization sharply critical of Alcoholics Anonymous. He based his program on cognitive-behavioral techniques influenced by the rational-emotive therapy of Albert Ellis. RR uses the Addictive Voice Recognition Technique, which helps the addicted person recover on his or her own by recognizing and controlling compulsive thoughts and desires. An RR participant defeats addiction by rational self-control rather than spiritual change. RR self-help groups meet once a week and participants discuss how to control irrational beliefs.

In the mid-1990s, Trimpey publicly denounced all self-help groups and treatment centers (including RR groups), and RR became an individual treatment program. The former RR self-help groups broke off and changed its name to SMART Recovery. SMART intends to provide an alternative to AA but is not as explicitly anti-AA as RR. Like RR, SMART views addiction as a learned behavior that can be changed using cognitive-behavioral principles. SMART recommends abstinence for its participants, but acknowledges that all of its members do not share this goal. SMART explicitly acknowledges science as the ultimate authority, adapting its

program to match research findings in relapse prevention, motivational enhancement, stress management, mood management, and other areas.

Moderation Management. In contrast to the abstinence-only programs, Moderation Management (MM) supports moderate use as a goal for its members. MM explicitly targets beginning stage problem drinkers, rather than seriously alcohol-dependent individuals. MM views non-dependent problem drinking as a bad habit, one controllable by following a nine-step cognitive-behavioral change program. Participants are encouraged to complete a 30-day abstinence period and then evaluate the positive and negative aspects of alcohol in their lives.

Overall, research indicates that being actively involved in a support group significantly improves one's chances of remaining clean and sober, but which mutual-aid support group one attends is not as important. Provided one participates in a mutual-aid support group, his or her religiosity does not directly influence the chances of remaining sober. Involvement in a group directly increases the amount of time one stays clean and sober (Atkins, 2007).

See also **Alcoholism: Abstinence versus Controlled Drinking; Models of Alcoholism and Drug Abuse; Women and Substance Abuse.**

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TRADITIONAL DYNAMIC PSYCHOTHERAPY

Dynamic psychotherapy is the term for the various psychological treatments, primarily talking treatments, intended to modify and ameliorate behaviors based on inner conflicts (e.g., "Should I study for the test or cheat?") and/or interpersonal conflicts (difficulties with others). These techniques range from those intended primarily to support individuals, lending them the therapist's strength or understanding ("If you do that you'll get in trouble. Have you thought of handling it this way?"), to helping patients reach their own understanding of the origins and implications of their behaviors. The application of these techniques to the treatment of alcoholics and substance abusers is supported by the high incidence of co-occurrence of psychiatric illness—in several studies, 70 percent—some of which may play a role in initiating or maintaining the behavior. It has been suggested that for some substance abusers, the use of illicit compounds is a misguided attempt at self-medication. Often, psychotherapy must be provided in conjunction with other treatments—pharmacologic, such as disulfiram for alcoholics or methadone for heroin abusers; self-help groups, such as Alcoholics Anonymous; or family or group psychotherapy.

Psychotherapy is based on the assumption that the patient will think and talk about ideas and feelings rather than acting upon them. This may prove particularly difficult for substance abusers who often have little sense of what they feel, other than generalized pain, and who are used to action and immediate gratification. Therefore, treatment, particularly at the beginning, must take place within a

structure that both supports and helps control impulsive behavior. Sometimes, treatment starts in a hospital or other residential setting; often, it is accompanied by regular drug testing. After the agreement to start therapy and setting goals, therapist and patient meet once to several times a week. As trust is developed between patient and therapist, the therapist can expect less lying and less denial of difficulties; treatment can, if indicated, begin to move from support toward expression of feelings—toward identification of conflicts and the understanding of their origins. Initially the therapist listens, struggling to understand the patient's inner experience and its meaning. The therapist then attempts to help patients to understand what they have presented, with appropriate changes and qualifications based on further information provided by the patient. Important issues to be explored in treatment include current relationships (with spouse, children, friends, coworkers), past relationships (with parents and other family), and the relationship within the treatment between the patient and the therapist. Often, the difficulties and distortions within this relationship mirror past and current relationships and may be used to help the patient see the nature and impact of the past on current behaviors.

Treating substance abusers can be frustrating for therapists; there are many slips with return to drug use, and patient behavior is often calculated to make the therapist angry and to give up. It is essential that therapists who make the attempt carefully monitor their own feelings so that they do not interfere with the treatment itself. It is also important to remember that when properly done, treatment can make the difference between suffering with chronic problems and successful adaptation. This is particularly true when substance abuse is accompanied by other psychiatric disease and/or disability.

See also **Epidemiology of Alcohol Use Disorders; Epidemiology of Drug Abuse; Models of Alcoholism and Drug Abuse.**

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TWELVE-STEP AND DISEASE MODEL APPROACHES

Twelve Step Facilitation, or TSF, is a manual-guided, twelve-step based treatment program that was developed for use in Project MATCH (Matching Alcoholism Treatments to Client Heterogeneity), a multicenter study examining patient-treatment matching for three different psychotherapies for alcohol dependence. TSF includes a range of interventions that are organized into a "core" program, an "elective" program, and a "conjoint" program. Thus, while the primary goal is facilitating the individual's relationship to self-help groups and fellowships such as Alcoholics Anonymous (AA), it is also an individual professional treatment and has no official relationship with AA or other such groups.

TSF is a structured intervention whose sessions follow a prescribed format. Each session begins with a review of the patient's recent efforts toward recovery, including any twelve-step meetings attended (and reactions to them), episodes of drinking or drug use versus sober days, urges to drink or use, reactions to any readings completed, and any journaling that the patient has done. The second part of each TSF session consists of presenting and discussing new material drawn from either the core, elective, or conjoint programs. Session guidelines and checklists are provided. These can be used by therapists to conduct TSF sessions, as well as by those who wish to monitor sessions to assess treatment fidelity. Each session ends with a wrap-up that includes the assignment of recovery tasks, which may include readings, meetings to be attended, and other behavioral work that the patient agrees to undertake between sessions. Most TSF topics include client handouts that are used either in-session or assigned as recovery tasks. The Twelve Step Facilitation Handbook (1998) includes troubleshooting guides for each topic that help practitioners anticipate and deal with potential issues that may arise in the course of treatment.

The TSF core program includes the following five topics: introduction and assessment; acceptance;

people, places, and routines; surrender; and getting active. The elective program is composed of the following five topics: genograms, enabling, emotions, moral inventories, and relationships. There is also a two-session conjoint program, consisting of the topics of enabling and detaching, which can be used if the client has a significant other who is willing to participate in treatment. Finally, TSF includes a termination session with its own format.

In implementing TSF, the therapist (or "facilitator") employs a variety of therapeutic techniques, including education and discussion, role-playing, confrontation, reinforcement, and coaching.

Patients need not necessarily be dependent on either alcohol or drugs to benefit from a twelve-step oriented treatment; rather, they must merely satisfy the basic criterion for becoming a member of a twelve-step fellowship, as set forth by Alcoholics Anonymous, namely, "a desire to stop drinking," or to stop using drugs (Alcoholics Anonymous, 1981, p. 139). Twelve-step fellowships advocate abstinence, as opposed to the controlled use of alcohol or drugs, as their goal. They do so, however, as a matter of practicality, as opposed to taking a moral stance on drinking per se. AA is for those who have already tried controlled drinking but have been unsuccessful in this effort. Bill Wilson, a cofounder of AA, put it this way: "We do not like to pronounce any individual as alcoholic, but you can quickly diagnose yourself. Step over to the nearest barroom and try some controlled drinking. Try to drink and stop abruptly. Try it more than once. It will not take long for you to decide, if you are honest with yourself about it" (Alcoholics Anonymous, 2001, pp. 31–32). Twelve-step fellowships exist to provide support and advice, and to facilitate the personal growth of individuals whose own efforts to control their use of alcohol and/or drugs have failed and whose lives have become increasingly "unmanageable" as a consequence of substance abuse.

In the years since the inception of AA, its twelve-step program and philosophy have been applied to a variety of addictive behaviors, such as smoking, gambling, and overeating. Mutual-support fellowships now exist for individuals seeking support in overcoming loss of control in each of these areas. AA conducts periodic surveys of its membership. As of 2006, AA estimated that there were 52,050 AA groups in the United States, with a membership totaling 1,069,000 people. Globally, it estimated that there were 106,202 groups, with a total membership of 1,867,000 people (Alcoholics Anonymous, 2006). These are likely underestimates, however, given that AA is decentralized and has no formal membership requirements.

"EARLY" RECOVERY

Based on an assessment of a patient's lifestyle, prior treatment experiences, periods of sobriety, and circumstances surrounding relapse, an individual treatment plan is devised, typically including one or more elective topics plus the core TSF program. Broadly speaking, what could be called "early" recovery can be broken down into three components: acceptance, surrender, and getting active in a twelve-step fellowship.

"Acceptance" refers to the process in which the individual overcomes "denial"—the personal belief that one does not have a substance abuse problem, or that one can effectively and reliably control drinking or drug use. It is captured in the first step of AA: "We admitted we were powerless over alcohol—that our lives had become unmanageable" (Alcoholics Anonymous, 2001, p. 59). Recovery can therefore be thought of as beginning with an epiphany: The realization that one has in fact lost the ability to control his or her use of alcohol or drugs, and that as a consequence life has become progressively more unmanageable. This is a significant insight, given that previously the individual may have held onto the idea that he or she could effectively control use, and that the consequences of alcohol or drug use were not significant.

Acceptance leads to surrender, which has two components: (1) hope that one can in fact reverse the process of powerlessness and unmanageability, and (2) the belief that individual willpower alone is an insufficient force for creating sustained sobriety and restoring manageability to one's life. The concept of surrender is embodied in Steps 2 and 3: "Came to believe that a Power greater than ourselves could restore us to sanity;" and "Made a decision to turn our will and our lives over to the care of God as we understood Him" (Alcoholics Anonymous, 2001, p. 59).

Steps 2 and 3 have a spiritual aspect, to the extent that hope is arguably a spiritual concept, and also by virtue of the fact that the third step asks the individual to believe in a "higher power." Many

people choose to think of this higher power as God, though even Bill Wilson consistently maintained that the higher power one chooses to believe in can just as well be AA itself and the power of fellowship. As Wilson put it, one key to recovery was to be found in humility: "This is the how and why of it. First of all, we had to quit playing God" (Alcoholics Anonymous, 2001, p. 62). Recovery, in other words, requires a willingness to place one's fate in the hands of something other than one's individual willpower.

Given the cognitive leap that acceptance and surrender represent, they lead in turn to the logical conclusion that the only sane alternative to continued chaos, loss, and accumulating negative consequences is to abandon willpower, turning instead to others—to become active in a twelve-step fellowship consisting of others who share the same goal of abstinence from alcohol or drugs.

As important as insight is, alone it is not sufficient for recovery, and that is where the concept of getting active comes in. Surrender implies not only a cognitive shift but a willingness to take action, and specifically to embrace the twelve steps as a guide for recovery and spiritual renewal. As much as they are programs of insight and spiritual renewal, AA and Narcotics Anonymous (NA) are also programs of action and lifestyle change.

Surrender and getting active follow acceptance and represent the individual's commitment to making whatever changes in lifestyle are necessary to sustain recovery. This requires action, including frequent attendance at AA or NA meetings, becoming active in meetings, reading AA or NA literature, getting a sponsor, making AA or NA friends, and replacing people, places, and routines that have become associated with substance abuse, and therefore represent a threat to recovery, with alternative relationships and habits of living. In TSF, the action and commitment that are the hallmarks of surrender are guided to some extent by the facilitator; but they are also heavily influenced by individuals the patient encounters and begins to form relationships with within twelve-step fellowships.

ADVANCED RECOVERY

Twelve-step fellowships regard spirituality as a force that provides direction and meaning to one's life, and they equate spiritual awakening with a realignment of personal goals, specifically a movement away from radical individualism and the pursuit of the material, and toward community and the pursuit of serenity as core values.

The twelfth step of AA states: "Having had a spiritual awakening as the result of these steps, we tried to carry this message to alcoholics, and to practice these principles in all our affairs" (Alcoholics Anonymous, 2001, p. 60). AA goes on to define what it means by spiritual awakening: "When a man or a woman has a spiritual awakening, the most important meaning of it is that he has now become able to do, feel, and believe that which he could not do before on his unaided strength and resources alone" (Alcoholics Anonymous, 1981, p. 106). This spiritual awakening comes, in time, as a result of involvement in the fellowship and "working" the twelve steps.

The process through which spiritual awakening is ultimately achieved is founded on a commitment to honesty and humility. This includes being honest with one's self and others, not only regarding alcohol and drug use, but also regarding such things as the harm that addiction has done (the "moral inventory"), plus ongoing vigilance regarding one's own character flaws. The individual in the advanced stages of recovery is someone who is always willing to acknowledge a fault and make amends for harm done, and who has discovered that giving to others—through sponsorship, for example—also supports one's own recovery. In this regard, twelve-step recovery has been likened to a form of spiritual conversion (Fowler, 1993).

Twelve-step fellowships are optimistic: "Rarely have we seen a person fail who has thoroughly followed our path" (Alcoholics Anonymous, 2001, p. 58). They believe that recovery leads to a profound reevaluation of how one relates to others, one's personal goals, and one's sense of purpose and meaning in life. They also accept the reality that abstinence is a goal that is rarely achieved without instances of either "slips" (single episodes of drinking or drug use) or "relapses" (a return to full-blown addiction). This attitude is reflected in the following statement, often quoted by AA members, from "the Big Book" (*Alcoholics Anonymous*): "The principles we have set down are guides to progress. We claim spiritual progress rather than spiritual perfection" (Alcoholics Anonymous, 2001, p. 60).

It is in this spirit that alcoholics and addicts are equally welcomed at meetings, whether they have one day or twenty years of sobriety.

THE EFFICACY OF TWELVE-STEP TREATMENT

TSF has been found to be effective in producing significant and sustained reductions in alcohol use lasting as long as 36 months after treatment (Project MATCH Research Group, 1997; Project MATCH Research Group, 1998). TSF has also been applied using a group format as an aftercare treatment with similar efficacy (Seraganian et al., 1998). In a study of depressed veterans with co-occurring substance use disorders and depression, TSF was correlated with improvement in substance use outcomes (Glassner-Edwards et al., 2007). When combined with the drug disulfiram, TSF was found to be effective in reducing cocaine and alcohol use (Carroll et al., 1998).

A significant finding from Project MATCH, which has been supported by other research, is a correlation between attendance at twelve-step meetings and abstinence from alcohol and drug use (Fiorentine, 1999). Greater involvement in twelve-step fellowships (e.g., getting a sponsor, taking on responsibilities) has also been found to correlate positively with recovery (Emrick, 1993). Finally, further analysis of Project MATCH data found that among patients whose social network (i.e., family and friends) supports drinking, TSF was associated with fewer drinking-associated consequences than two comparison treatments (Wu & Witkiewitz, 2008). Following a peer review, TSF was selected for inclusion in the National Registry of Evidence-Based Programs and Practices.

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TREATMENT, PHARMACOLOGICAL APPROACHES TO

This entry includes the following essays:

AN OVERVIEW

Pharmacological agents can be used for several purposes in the treatment of drug and alcohol addiction. These include the alleviation of acute withdrawal symptoms, the prevention of relapse to drug or alcohol use, and the blocking of the euphorigenic effects of drugs of abuse. Various medications are used in the treatment of addiction to alcohol, opiates, cocaine, tobacco, and sedatives.

ALCOHOLISM

Detoxification. Alcohol is currently one of the most widely used of the mood-altering substances. Habitual alcohol use is associated with the development of tolerance and physiological (physical) dependence. Tolerance refers to a decrease in susceptibility to the effects of alcohol following chronic alcohol use, which results in the user consuming increasing amounts of alcohol over time. Physical dependence can be conceptualized as a physiological state in which the recurrent administration of alcohol is required to prevent the onset of withdrawal symptoms. Symptoms of alcohol withdrawal include irritability, tremulousness, anxiety, sweating, chills, fluctuations in pulse and blood pressure, diarrhea, and, in severe cases, seizure. These symptoms generally begin within 24 hours following the last use of alcohol, peak within 48 hours, and subside over several days.

Pharmacotherapy for alcohol withdrawal includes the use of agents such as benzodiazepines and barbiturates, which are cross-tolerant with alcohol. These agents attenuate the symptoms of withdrawal and result in decreased arousal, agitation, and potential for seizure development. Medication is provided in doses that are sufficient to produce mild sedation and physiological stabilization early in the withdrawal period; this is followed by a gradual dose reduction and then discontinuation over the next one to two weeks. Currently, benzodiazepines are the agents of choice for the treatment of alcohol withdrawal because of the relatively high therapeutic safety index of these medications, their ability to be administered both orally and intravenously, and because of their anticonvulsant properties. Barbiturates can be used in a similar fashion but they have a lower therapeutic index of safety than do benzodiazepines.

Other medications used to treat alcohol withdrawal include clonidine and carbamazepine. Clonidine is an antihypertensive agent (i.e., it lowers blood pressure) that has been used in the treatment of drug withdrawal states and chronic pain. This medication decreases autonomic hyperactivity (i.e., it lowers an increased pulse and blood pressure) but it does not have the anticonvulsant properties of the benzodiazepines or barbiturates. Carbamazepine, an anticonvulsant, has also been employed in the treatment of alcohol withdrawal. Neither medication is habit-forming and thus may be of value in the treatment of alcohol withdrawal. Another anticonvulsant that may be useful in the treatment of alcohol withdrawal is valproic acid, though there is less evidence of its value for this indication than there is for carbamazepine.

Antidepressants. Depressive symptoms are noted in many alcoholics at the time that they enter treatment. Because of the frequent co-occurrence of depression and alcoholism, the use of antidepressants could be potentially useful in this population. Several studies have demonstrated the favorable effects of antidepressants on alcohol consumption,

but several other studies have not. Tricyclic antidepressants such as imipramine and desipramine inhibit the reuptake of norepinephrine and serotonin in nerve terminals. The serotonin reuptake inhibitors (blockers) sertraline (Zoloft) and fluoxetine (Prozac) have shown a lack of efficacy in the treatment of major depression in alcoholics. Although antidepressants are not routinely administered to all recovering alcoholics, many physicians consider prescribing such medications to alcoholic patients if depressive symptoms do not resolve after several weeks of abstinence, or if a mood disorder was present prior to the onset of (alcohol) abuse.

Anxiolytics. Used to decrease anxiety, anxiolytics include benzodiazepines such as chlordiazepoxide (Librium) and diazepam (Valium), and azaspirodecadiones such as buspirone (BuSpar). Both classes of medication have been investigated for use in alcohol dependence. Early studies supported the use of benzodiazepines in recovering alcoholics with claims of decreased alcohol craving and consumption after chlordiazepoxide administration. Other controlled trials refuted this, however, and many physicians question the safety of using benzodiazepines in this population. The azaspirodecadiones such as buspirone are nonaddictive medications that have been marketed for the treatment of anxiety. Although few controlled trials have been conducted to evaluate the effect of buspirone on alcohol consumption in humans, there is some evidence of beneficial effects in anxious alcoholics. Animal studies have also demonstrated decreased alcohol consumption after treatment with this agent. Unlike benzodiazepines, buspirone is not known to be habit-forming and thus may be a promising agent for use in alcoholics.

Dopaminergic Agents. The effects of dopaminergic agents on the consumption of alcohol in animal studies have been conflicting because both agents that augment dopaminergic activity and those that diminish it have been noted to decrease alcohol consumption. In humans there are also conflicting findings, with some evidence that both dopamine agonists and antagonists reduce drinking behavior.

Opioid Antagonists. Opioid antagonists are competitive antagonists of opioids at opiate receptors. They include naloxone, which can be used intramuscularly or intravenously to rapidly reverse opiate intoxication and naltrexone, which is prescribed orally to prevent or reverse intoxication from opioids and for the treatment of alcohol dependence. Unlike opioids these medications are not habit-forming and clearly have a place in the treatment of alcohol-dependent patients. A variety of studies have demonstrated a reduction of alcohol consumption or self-administration by animals treated with these agents. In human subjects naltrexone administered as an adjunct to substance-abuse treatment has resulted in a decreased rate of alcohol consumption. In addition, those patients who did experience a *slip* were less likely than those who were not treated with naltrexone to suffer a complete relapse to alcohol use. Like the oral medication, an extended release intramuscular injectable formulation of naltrexone is approved for treatment of alcohol dependence. The long-acting formulation may offer some advantages over oral administration. Keeping plasma levels relatively constant through slow release of naltrexone may keep therapeutic levels of the medication constant as well as reduce the occurrence of adverse effects such as nausea that occur following initial oral doses of naltrexone. In addition, depot naltrexone allows for less frequent dosing, which can contribute to better medication compliance.

Aversive Agents. Aversive agents are medications that are used to decrease alcohol consumption by creating an adverse reaction following alcohol use. They include disulfiram, calcium carbimide, and metronidazole (Flagyl). Levels of acetaldehyde, a toxic breakdown product of alcohol, accumulate when patients who are using disulfiram ingest alcohol. This results in symptoms of acetaldehyde toxicity including sweating, chest pain, palpitations, flushing, thirst, nausea, vomiting, headache, difficulty breathing, hypotension (low blood pressure), dizziness, weakness, blurred vision, and confusion. Symptoms may begin within minutes following alcohol ingestion and may last from thirty minutes to several hours. The use of disulfiram is based upon the premise that the fear or actual experience of this adverse event may serve as a deterrent to alcohol use. Despite its toxicity, disulfiram has been used safely by thousands of recovering alcoholics since its introduction in 1948. Supervised voluntary use of the medication as an adjunct to other rehabilitative therapy has resulted in reduced alcohol consumption and decreased alcohol-related criminal behavior among alcohol-dependent patients.

Compliance is the key to successful use of disulfiram in alcohol dependence, since patients need only discontinue using disulfiram if they wish to resume drinking. Indeed, in an unsupervised setting, disulfiram administration shows no superiority over placebo on outcome measures related to alcohol use. Methods that have been investigated to improve compliance include surgical implants of disulfiram, reinforcement by providing a reward for compliance, and contingency management techniques. Although surgical implants have met with little success, the other two methods have demonstrated various degrees of efficacy.

Reduction in alcohol use and an increase in alcohol-free days of alcohol-dependent individuals can be improved by treatment with topiramate, an anticonvulsant medication that stimulates the GABA pathway and blocks glutamate receptors. Topiramate may decrease the reinforcing effect of alcohol and other drugs such as cocaine and nicotine, based on its glutamate-mediated effects on the mesolimbic dopamine system. In addition it may contribute to abstinence by decreasing neuronal sensitivity. At a low dose, topiramate use may be effective in patients abusing alcohol while being maintained on therapy with buprenorphine or methadone and who do not need medical detoxification for alcohol. Topiramate is not approved by the U.S. Food and Drug Administration (FDA) for the treatment of alcohol dependence. Acamprosate is another medication that has shown efficacy in relapse prevention in alcohol dependence. Acamprosate attenuates alcohol desire or craving by normalizing the dysregulation of NMDA, glutamate-mediated excitation that occurs in alcohol withdrawal and the first 4 to 6 weeks of abstinence. Acamprosate is FDA approved for use in alcohol dependence and the side effects, primarily diarrhea, are generally well tolerated.

OPIOID DEPENDENCE

The opioids include opiates, which are drugs derived from the opium poppy (*Papaver somniferum*) as well as those synthesized to produce similar narcotic effects. Opium has been used as a medicinal substance for at least 6,000 years. Widespread abuse of opiates was noted by the eighteenth century with the smoking of opium in Asia; since the start of the twenty-first century in 2000 prescription opiates such as OxyContin and hydrocodone have surpassed heroin as the major opiates of abuse in the United States. Pharmacotherapy for opiate dependence may be employed both during the acute withdrawal syndrome and later to maintain abstinence from illicit opioids (e.g., heroin).

Acute Opioid Withdrawal. The syndrome of acute withdrawal from opiates varies in regard to the opiate of abuse. The time of onset, the intensity, and the duration of withdrawal symptoms depend on several factors including the half-life of the drug, the dose, and the chronicity of use. Heroin is a relatively short-acting agent; symptoms of withdrawal often begin within eight to twelve hours after the last use. Early symptoms include craving, anxiety, yawning, tearing, runny nose, restlessness, and poor sleep. Symptoms may progress to include pupil dilation, irritability, muscle and bone aches, piloerection (goose bumps—thus the term *cold turkey*), and hot and cold flashes. Peak severity occurs 48 hours to 72 hours after the last dose and includes nausea and vomiting; diarrhea; low-grade fever; increased blood pressure, pulse, and respiration; and muscle twitching. The opiate withdrawal syndrome following chronic heroin use can last seven to ten days. With longer-acting agents such as methadone, a similar constellation of symptoms can occur though they begin later, peak on the third to eighth day, and persist for several weeks.

A variety of medications can be used in the treatment of acute opiate withdrawal. The most common method is to use opiates alone. A dose high enough to stabilize the patient is administered on the first day and then gradually tapered over one to two weeks. Generally, long-acting opiates such as methadone are employed, but any opiate can be used.

Other medications used for opiate withdrawal are clonidine and buprenorphine. Clonidine is an alpha-2 adrenergic agonist that is commonly employed as an antihypertensive medication. It is active on central nervous system (CNS) locus coeruleus neurons in the same areas at which opiates exert their effects. Clonidine appears most effective in decreasing symptoms such as elevation of pulse and blood pressure and may be less effective in relieving other symptoms of withdrawal. The major side effects of clonidine are orthostatic hypotension (decreased blood pressure when rising

from a sitting or lying position) and sedation. Rapid detoxification can occur through the combined use of clonidine with opiate antagonists such as naltrexone. This treatment can decrease the time required for the detoxification process to two to three days. Opiate addicts can be stabilized on buprenorphine, a mixed opioid agonist/antagonist with minimal discomfort and then withdrawn over five to seven days with less severe withdrawal symptoms than those associated with methadone withdrawal. Lofexidine and guanfacine are alternative alpha-2 adrenergic agonists that are under investigation for the management of opioid withdrawal. Lofexidine appears to be as effective as clonidine; however, it may be more suitable than clonidine for use in outpatient settings since some studies have shown fewer adverse effects, such as hypotension, with its use.

Antagonists. Opiate antagonists such as naloxone and naltrexone compete with opiates for CNS opioid receptors. Naloxone has a short half-life (two to three hours) and is generally employed on a short-term basis to reverse acute opiate intoxication. Naltrexone has a longer duration of action (approximately 24 hours) and is used as a long-term maintenance medication to inhibit euphoria in opioid addicts. Although not approved for use in the treatment of opioid dependence, long-acting naltrexone can be of use in this disorder. Oral opioid antagonist medications have been used with relative safety since 1975. Clinically, side effects of naltrexone may include mild dysphoria and elevation in cortisol and beta-endorphin levels; no withdrawal syndrome has been noted following its discontinuation. Oral naltrexone is generally administered three to four times a week at an average dose of 50 milligrams per day. The long-acting formulation is administered monthly. Despite its advantages, many opioid addicts resist therapy with naltrexone, and even in the most successful programs, six-month retention rates may range from only 20 to 30 percent. The addition of psychosocial interventions such as counseling and contingency-management programs is helpful. When these interventions are added, naltrexone has been noted to be particularly effective in selected groups including health care professionals, business people, and prisoners on work-release programs.

Methadone Maintenance. Methadone is a safe and effective treatment that has been used to treat opioid dependence since 1965. Heroin addicts easily adapt to using this long-acting opiate that possesses all of the physiological characteristics of heroin. When taken orally, methadone may have less abuse potential than heroin, but the onset of its CNS effects are slower and its tendency to induce euphoria is generally less than that of intravenous or inhaled heroin. In addition it has a longer half-life than heroin and if it is administered daily, tissue levels accumulate thereby decreasing withdrawal symptoms that occur between doses and that may lead to repeated opiate use. Methadone maintenance can be of benefit for addicts who have difficulty adjusting to a drug-free lifestyle or for those who have been unsuccessful with other forms of treatment. However, methadone maintenance is limited by the close regulation that it gets by the DEA and FDA. This regulation leads to the patient inconvenience of attending a dispensing facility 6 days per week for at least the first 3 to 6 months of treatment and to substantial administration costs from the nurses and pharmacists needed to provide this dispensing.

During maintenance therapy methadone is initiated at a low dose and then gradually increased to higher doses, which are associated with decreased opiate craving and secondary illicit opiate use. With methadone maintenance treatment many patients show significant decreases in illicit drug use, depression, and criminal activity, and they demonstrate increased employment. Therapy that is provided for extended periods of time and in the context of other psychosocial services has been associated with the highest success rates.

Buprenorphine. Buprenorphine is a mixed opioid agonist/antagonist that has been used experimentally since 1983 and clinically since 2001 as a maintenance medication for opioid dependence. As with methadone, maintenance treatment consists of daily administration of buprenorphine. At low doses, buprenorphine has agonist effects at opioid receptors and suppresses withdrawal symptoms. At higher doses antagonistic effects can occur, which act to block the reinforcing properties of the drug, thus lowering the potential for it to be abused. Buprenorphine maintenance has been associated with

good treatment retention, decreased illicit opiate use, and a relatively mild withdrawal syndrome. Furthermore, a combination therapy of buprenorphine and naloxone is available as Suboxone. Suboxone has made office-based maintenance treatment of opiate dependence possible without the regulatory and administrative costs and complications of methadone maintenance. Any physician can prescribe Suboxone from his office after a relatively brief training from an approved source and an approval process by the Drug Enforcement Administration. This has led to a vast expansion of the treatments available with treatment access now possible in rural areas that had a great amount of prescription opiate abuse. It has also provided capacity expansion from about 220,000 methadone-treated patients to more than about 500,000 patients on either methadone or Suboxone in the United States. This expansion has benefited many who would not accept methadone maintenance or lived in areas that did not have methadone treatment. Overall this expansion has been essential with the growth in prescription opiate abuse since 2000.

COCAINE DEPENDENCE

Cocaine abuse increased markedly beginning in the 1970s, and by 1984 more than 20 million Americans reported that they had tried cocaine. In addition to psychotherapy and other traditional approaches to substance abuse treatment, a variety of medications may be of benefit to cocaine abusers. However, no medications have been approved by the FDA for this indication.

Pharmacotherapy for cocaine abuse can be employed to address specific symptoms that occur during the cocaine-withdrawal syndrome. Gawin and Kleber (1986) identified three phases in the cocaine abstinence syndrome. The crash phase generally begins soon after cocaine use ends and may last up to four days. Symptoms experienced at this time can include depression, suicidal ideation, irritability, anxiety, and intense cocaine craving. Sedatives such as alcohol and heroin can be used by addicts to alleviate these symptoms. The second, or withdrawal phase, can last two to ten weeks and is characterized by anxiety, depression, inability to experience pleasure, and increased cocaine craving. The third, or extinction phase, can last three to twelve months; during this phase, cocaine craving may continue as well as increased susceptibility to relapse in response to environmental cues.

Pharmacotherapy for cocaine dependence can be used to alleviate symptoms experienced during the cocaine abstinence syndrome. During the crash period, early symptoms such as anxiety and insomnia may be relieved by benzodiazepines such as chlordiazepoxide. Antipsychotics can also be helpful during this period to alleviate psychotic symptoms such as paranoia.

Other agents that can be used on a short-term basis include dopaminergic agents such as bromocriptine and amantadine. Some investigators postulate that CNS dopamine can be depleted by chronic cocaine use. Dopaminergic agents can be used to augment CNS dopaminergic function and various dopaminergic agents such as amantadine, bromocriptine, and L-dopa have been employed for this purpose. Although few long-term, double-blind, placebo-controlled studies have been conducted, several studies have supported the use of dopaminergic agents, such as amantadine, as anti-craving medications during withdrawal.

Antidepressants can be helpful during the withdrawal and extinction stages of cocaine abstinence. One controlled and several uncontrolled studies in recovering cocaine addicts suggested that the tricyclic antidepressant desipramine might have decreased cocaine use and craving. Other antidepressants investigated in pilot studies included fluoxetine, imipramine, doxepin, and trazodone. Antidepressants can take several weeks to begin to alleviate symptoms of depression or craving, however, and some cocaine addicts may drop out of treatment during this period. These patients can benefit from initiation of treatment with a short-term medication (such as a dopaminergic agent) followed by long-term treatment with an antidepressant. As with every treatment, however, no firm conclusions are warranted about any agent until it has been tested in a controlled clinical trial that has been replicated at least once.

Pharmacotherapy can also be helpful for patients with psychiatric diagnoses other than cocaine dependence. In some patients cocaine abuse may be an attempt at self-medication to address the discomfort of depression or other psychiatric disorders. Patients with major depressive disorder or bipolar disorder may respond to therapy with antidepressants

or lithium, respectively, and those with attention deficit disorder may benefit from the cautious use of low doses of a stimulant medication.

In summary, antipsychotics and benzodiazepines can be used to alleviate symptoms of acute cocaine withdrawal, whereas tricyclic antidepressants and dopaminergic agents can be helpful in the long-term treatment of cocaine withdrawal. Pharmacotherapy should be considered an adjunct to other forms of rehabilitative therapy during the long-term treatment of the cocaine-dependent patient.

TOBACCO DEPENDENCE

The main reason to quit smoking cigarettes is its powerful association with lung cancer, emphysema, and other medical problems. Yet nicotine, the active ingredient in cigarettes, is another drug that is associated with pleasant effects and with withdrawal discomfort, thereby making it an extremely addictive drug. Nicotine replacement therapy is a commonly used pharmacological treatment for tobacco dependence and is administered in the form of a gum, a patch, a lozenge, an inhaler, or a nasal spray. Providing cigarette smokers with nicotine replacement will help them avoid the health risks associated with smoking cigarettes. One problem with nicotine gum is that it is difficult to chew correctly and therefore people need to be trained to chew it correctly to derive the therapeutic effect and minimize adverse effects. The patch has been available since the early 1990s and was developed for placement on the skin, facilitating automatic release of nicotine. The nicotine inhaler and nicotine nasal spray are available by prescription and provide fast delivery of nicotine through the mouth and nose, respectively. Antidepressants like bupropion have also been quite successful in alleviating withdrawal symptoms from nicotine. Bupropion (Zyban) was approved by the FDA for this indication. Second-line medications for smoking cessation include antidepressants like nortriptyline. Detoxification from nicotine may also be facilitated with the medication clonidine, which is also used to help alleviate opiate withdrawal symptoms. Varenicline (Chantix), a *partial agonist* of the $\alpha_4\beta_2$ subtype of the *nicotinic cholinergic receptor*, is also FDA approved for smoking cessation based on evidence that it helps to reduce withdrawal symptoms and craving as well as reduce the level of smoking satisfaction.

SEDATIVE DEPENDENCE

Current treatments for sedative dependence include detoxification agents rather than anticraving agents. Detoxification is accomplished by tapering the dosage of benzodiazepines over two to three weeks. Carbamazepine, an antiseizure medication, has been shown to relieve alcohol and sedative withdrawal symptoms including delirium tremens. Agents that block the actions of benzodiazepines are promising as a maintenance or anticraving medication to help promote abstinence from sedative use.

PHARMACOTHERAPY

Medications must be accompanied by psychological and social treatments and support—they do not work on their own. Moreover, medications to block illicit drug effects in the brain are of little use if the patient does not take them. More research is needed to identify potential medications, but the clinical evaluation must recognize the need for psychosocial as well as neurobiological intervention. Without this integration the work to develop more effective treatments for the difficult problem of drug abuse and dependence cannot move forward.

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ANTICONVULSANTS

Anticonvulsants are medications approved to treat seizure disorders. Several anticonvulsants influence the reinforcing effects of psychoactive substances and have been used in the treatment of addictive disorder. These mechanisms appear to involve both gamma-amino butyric acid (GABA), the most abundant inhibitory neurotransmitter, and glutamate, the most abundant excitatory neurotransmitter in the brain. It has been hypothesized that anticonvulsants decrease the positive reinforcing effects of abused substances, such as reward and craving, by modulating dopamine neurotransmission through the facilitation of GABA neurotransmission. Perhaps more important, several anticonvulsants also appear to antagonize the glutamatergic activation and glutamate receptor upregulation associated with substance dependence and withdrawal. Thus, they influence the negative reinforcing effects associated with psychoactive substance withdrawal symptoms, especially that of ethanol and other depressants. Based on this general theoretical framework, there is a developing literature on the use of several anticonvulsants to treat alcoholism and other substance use disorders (SUDs). Here, the available evidence for the following anticonvulsants will be discussed: topiramate, carbamazepine, oxcarbazepine, divalproex, gabapentin, and lamotrigine.

Topiramate is thought to be a modulator of excitatory glutamatergic neurotransmission and a facilitator of the inhibitory GABA system. Strong evidence exists from two randomized, double-blind, placebo-controlled studies supporting the efficacy of topiramate for alcohol dependence: one single-site study with 150 patients (Johnson, Ait-Daoud, et al., 2003), and a more recent multisite, 14-week trial (Johnson, Rosenthal, et al., 2007). These studies reported a robust effect of topiramate compared to placebo in decreasing alcohol use, as indicated by multiple drinking outcomes such as percentage of heavy drinking days, secondary drinking outcomes, and a significant decrease in the liver enzyme, glutamyl transpeptidase (GGT), commonly elevated as a consequence of heavy alcohol use. In addition, these studies demonstrated that topiramate could be initiated safely and reliably in patients who are currently drinking heavily without the need to establish even a few days of abstinence before initiating treatment. Although some small-scale and open-label studies suggest that topiramate may promote abstinence from cocaine, nicotine, and MDMA, the evidence of its efficacy for these other addictions has yet to be established.

Carbamazepine has been tested for the treatment of alcohol withdrawal syndrome and for decreasing alcohol use in alcohol dependence. Carbamazepine suppresses withdrawal-induced kindling in limbic brain structures; it has reduced withdrawal symptoms and prevented alcohol withdrawal seizures in laboratory animals. Several studies, although not all, have documented its usefulness in the treatment of alcohol withdrawal. Available studies suggest that carbamazepine may have an advantage over benzodiazepines in the treatment of alcohol withdrawal because it decreases overall global distress. Preliminary indications also point to carbamazepine's usefulness in prolonging the time to relapse after detoxification (Malcolm, Myrick, et al., 2002). A small randomized trial evaluated the efficacy of carbamazepine for the treatment of alcohol dependence. Although this study indicated that carbamazepine did have some advantages over the placebo, in terms of the quantity of

alcohol use, the time to next use, and a faster return to vocational functioning, definitive studies establishing the efficacy of carbamazepine in treating alcohol dependence are still to be conducted (Mueller, Stout, et al., 1997). A recent comprehensive review of the available clinical trials for carbamazepine in cocaine dependence concluded that no evidence existed to support the efficacy of carbamazepine in treating it (Minozzi, Amato, et al., 2008).

Divalproex is another GABAergic, anti-kindling agent that has been found helpful in treating alcohol withdrawal and in decreasing alcohol use among patients with alcohol dependence, and those with comorbid bipolar disorder (Salloum, Cornelius, et al., 2005). In addition, small-scale pilot studies have found divalproex helpful in treating cocaine use. However, no large-scale multi-site studies have tested the drug for these conditions, and although available data suggest its usefulness in this context, definitive studies are still to be conducted to establish its efficacy in treating addictive disorders.

In summary, certain anticonvulsants seem promising for the effective treatment of alcohol withdrawal and for the promotion of abstinence and relapse prevention in alcoholism. They may be helpful in treating other addictions as well. Other anticonvulsants, such as gabapentin, oxcarbazepine, and lamotrigine, have also been of interest. Of the medications reviewed above, only topiramate has been tested in a large multi-site clinical trial. As some of the mentioned medications are also effective mood stabilizers, they may be suitable for treating co-occurring bipolar disorder in patients with alcoholism.

See also **Gamma-Aminobutyric Acid (GABA); Glutamate; Neurotransmission; Neurotransmitters.**

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ANTIDEPRESSANTS

Antidepressant drugs are a diverse group of medications that reduce the symptoms of clinical depression. The word *depression* is commonly used to describe a state of sadness, but health professionals describe illnesses very specifically in order to increase the precision of communication in research and clinical practice. For example, *major depression* is defined as a recurring problem characterized by severe and prolonged periods of depressed mood, often with other symptoms such as dejection, lack of energy, and inactivity. Major depression significantly interferes with everyday functioning in life. A similar illness, *dysthymia*, is a chronic mood state characterized by depression and irritability (dysthymia was once referred to as depressive neurosis). Depressive symptoms are also part of an important mood disorder called *bipolar disorder* (also known as *manic-depressive illness*), in which periods of depression alternate with periods of manic behavior. The signs and symptoms of depression or mood disorders may occur as part of other medical and psychiatric disorders. They may occur, for example, following stroke, as a result of endocrine disorders, or as a consequence of excessive drug use.

Antidepressants can also be useful in a number of medical and psychiatric disorders where depression is not the major feature. For example, some categories of antidepressants can be used to treat anxiety and panic disorders, and some are often

useful as adjunctive medications for chronic pain. Antidepressant drugs are not generally helpful for short-term depressed moods that are part of everyday life, or for the normal period of grief that follows the loss of a loved one. One drawback of antidepressant drug treatment is that it takes weeks for the full therapeutic benefit to appear. In addition, patients should not stop taking the drugs abruptly, because symptoms of withdrawal may appear. Instead, the use of these drugs should be discontinued very gradually. Because of the complexity of their effects, antidepressants are prescription drugs that should be taken only under the care and guidance of a physician.

Various categories of antidepressants have been developed over the years, and they are still being developed and tested. These categories include tricyclic antidepressants, monoamine oxidase (MAO) inhibitors, atypical antidepressants, and selective serotonin-reuptake inhibitors (SSRIs). In addition, lithium and some antiepileptic drugs have mood-stabilizing effects and are used in bipolar disorder. The chemical structures of some of these are shown below.

The tricyclic antidepressants, which have been used for many years in the treatment of depression, include such compounds as imipramine (Tofranil), nortriptyline (Aventyl), and desipramine (Norpramin). Most of the tricyclics can be given in a single dose at bedtime. The tricyclics, like other antidepressants, require a period of two weeks or more before they are fully effective. The tricyclics also have many side effects and a relatively narrow margin of safety, which means that they have adverse effects (some of which can be fatal) that appear at a dosage that is not very much greater than the therapeutic dosage. As a rule, physicians are cautious about prescribing tricyclic antidepressants if the patient appears to be at risk for suicide.

The monoamine oxidase (MAO) inhibitors are not commonly used because of their side effects and because they require certain dietary restrictions (e.g., patients are not allowed to eat liver, aged meats, most cheeses, red wine, or soy sauce). They include phenelzine (Nardil), isocarboxazid (Marplan), and tranylcypromine (Parnate). These antidepressants may be given in either the morning or the evening, depending on their effect on the patient's sleep.

The selective serotonin-reuptake inhibitors (SSRIs) are a newer, major category of antidepressant medications, and they are currently among the first-line drugs used to treat depression. Fluoxetine (Prozac), which is now available in generic form, has been a best-selling antidepressant since the mid-1990s. Other SSRIs include paroxetine (Paxil), sertraline (Zoloft), and escitalopram (Lexapro, Cipralex). The SSRIs have several advantages. They have less toxicity than the tricyclics or the MAO inhibitors, which is a significant factor in their popularity. They can also be used to treat bulimia and obsessive-compulsive disorder. Since insomnia is a common side effect of SSRIs, they are usually given as a single dose in the morning. The SSRIs can have other side effects, including sexual dysfunction, and they can be expensive. A growing number of SSRIs are available as generics, which has reduced the cost of treatment with these medications.

Another antidepressant, bupropion (Wellbutrin, Zyban), is a member of the "atypical" class. It is often a choice if SSRIs fail to work or have intolerable side effects (such as weight gain, which has been observed commonly with the SSRIs, but not with bupropion). Although lithium (Eskalith, Lithonate) is useful in treating bipolar disorder, it is not generally used for other types of depression. Lithium may have serious side effects, and it may be toxic at high dosages. Patients taking lithium should have regular blood tests to be sure that lithium levels are acceptable. Exposure to lithium in early pregnancy is associated with an increased frequency of birth defects, and the long-term use of lithium can damage kidney function. Some antiepileptic drugs (e.g., carbamazepine, valproic acid) are effective mood stabilizers and are often prescribed for the treatment of bipolar disorder.

Antidepressants can be used to treat depression associated with drug dependence and withdrawal, and some studies suggest that they may reduce drug intake. Alcoholics, for example, are often depressed, and other drug abusers often have depression as a comorbid problem. Some antidepressants may reduce cocaine use, but there are no proven, highly effective drug treatments for psychostimulant abuse. Bupropion (Zyban) is approved and widely used to treat nicotine dependence. SSRIs have been studied extensively as treatments for alcohol dependence.

Overall, the literature indicates that these medications may be beneficial for the subgroup of individuals with late-onset (after age 25) alcoholism. In contrast, there is evidence that these medications are either ineffective or counterproductive in reducing drinking or promoting abstinence in early-onset alcoholics.

In summary, antidepressants are an effective and important class of drugs, partly because of the high prevalence of the illnesses for which they are effective treatments. Antidepressants also can have a role in treating some kinds of substance abuse or dependence, and they may be useful for treating the depression that can occur with various kinds of substance abuse.

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ANTIPSYCHOTICS

ANTIPSYCHOTIC MEDICATIONS

Antipsychotic medications are any of a group of drugs, sometimes termed neuroleptics, used in the therapy of schizophrenia, organic psychoses, manic-depressive illness, and other psychotic illnesses. The prototype (so-called *typical*) antipsychotics (Figure 1) are primarily phenothiazines such as chlorpromazine (Thorazine), and butyrophenones such as haloperidol (Haldol). These antipsychotics tend to be tricyclic compounds with chemical substitution at R1 and R2, which determine the side effects and the potency of the drug.

A group of newer *atypical* antipsychotics was introduced in the 1990s: clozapine (Clozaril) (Figure 2), risperidone (Risperdal), olanzapine (Zyprexa), quetiapine (Seroquel), aripiprazole (Abilify), ziprasidone (Geodon), and paliperidone (Invega).

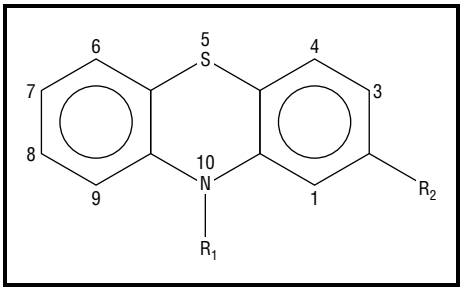

Figure 1. Chemical structure of an atypical antipsychotic.
ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

The antipsychotics often effectively treat positive symptoms of the psychotic disorders, such as hallucinations; these drugs have a lesser effect in managing negative symptoms, such as social withdrawal. All of the antipsychotics are effective although clozapine seems to be the most effective in patients who do not have a good response to the other drugs.

The older typical antipsychotics tend to produce adverse effects on movements, which must be balanced against their beneficial effects. Many of the newer atypical antipsychotics also have adverse effects, particularly weight gain and metabolic side effects (such as elevated blood glucose and triglyceride concentrations), which must also be considered in their use. Clozapine, although very effective, produces the

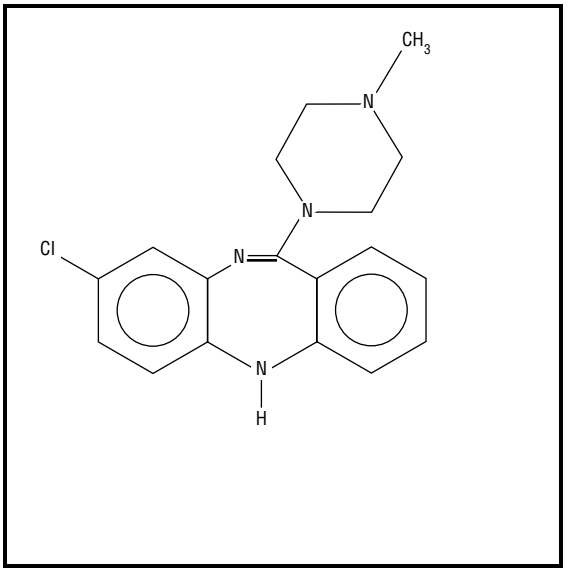

Figure 2. Clozapine—the first atypical antipsychotic.
ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

most severe side effects, which can include a potentially life-threatening suppression of white blood cells.

See also **Personality Disorders; Pharmacology; Research: Measuring Effects of Drugs on Behavior; Schizophrenia.**

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ALAN I. GREEN

AVERSION THERAPY

The method of treating alcoholics by pairing the consumption of alcohol with an aversive experience has been used since ancient times. In their review, Howard and co-workers (1991) cited several important examples from history and literature starting with the Romans, who used spiders or eels as an aversive effect in the bottom of wine cups to discourage the drinker. Benjamin Rush, one of the fathers of American psychiatry, reported a case of successful aversive treatment in 1815. In literature, Anton Chekhov in *A Cure for Drinking* and Anne Brontë in *The Tenant of Wildfell Hall* described individuals who experienced aversive treatment.

The first clinical use of aversion therapy in alcoholics was reported in 1930. The method was used in several countries over the subsequent decades. The method was first used in the United States in 1935 and became widely available in the subsequent decades.

The present entry concerns only chemical aversion therapy (CAT). The idea is that repeated pairing of alcohol and chemically induced nausea triggers a conditional response. The chemical agent commonly used is emetin.

Non-chemically induced nausea has been used with similar protocols. Electric aversion therapy has been applied in some studies with a similar outcome (Smith, Frawley, & Polisser, 1997). Another method is covert sensitization. In this form of treatment, imagined drinking episodes are repeatedly paired with nausea induced through noxious verbal suggestions (Miller & Dougher, 1984).

In the early days of disulfiram treatment, the drug was given in combination with alcohol. The aversive effect was regarded as beneficial for the long-term outcome of the patient. However, reports of severe or fatal disulfiram-ethanol reactions led to the abandonment of this procedure (Jabobsen, 1952). For the same reason, the use of disulfiram as an emetic agent in CAT was abandoned.

The protocol for CAT varies. A typical protocol, as described by Elkins (1991), consists of about five emetin sessions over an initial 10-day treatment phase. In addition, post-discharge reinforcement sessions are conducted, one after 30 and another after 90 days.

Many alcoholics display a conditioned response during CAT. This has been demonstrated using psychophysiological and behavioral indices (Elkins, 1991). Howard (2001) reported that positive alcohol-related outcome expectances were significantly reduced, whereas confidence that drinking could be avoided in various high-risk situations for alcohol consumption was increased following CAT. Patients prone to antisocial behavior appeared to be less susceptible to the CAT conditioning protocol.

As of 2008, the efficacy of CAT was not very well documented, with only two small, randomized studies available. Wallerstein (1957) evaluated the relative effectiveness of CAT, disulfiram, hypnotherapy, and milieu therapy. He found that 50 patients (80%) undergoing CAT completed treatment, compared to 47 (83%), 39 (64%), and 42 (62%) of disulfiram, hypnotherapy, and milieu therapy subjects, respectively. There were no significant differences between CAT and the other treatment options in retention or short-term outcome. Cannon and colleagues (1981) studied 20 patients who were randomized to CAT, shock aversion therapy, or a control group. At the six-month follow-up, CAT subjects had been abstinent for a mean of 170 days, while shock aversion therapy and control subjects were abstinent for 109 and 158 days, respectively. Group comparisons revealed that CAT subjects were abstinent for significantly more days than patients in the combined shock aversion and control groups. The significant differences disappeared at the one-year follow-up.

Among other studies, only one used a comparison group. Smith, Frawley, and Polisser (1991) compared 249 alcoholic inpatients that had undergone aversion therapy with patients from a national

treatment registry who did not receive aversion therapy. The patients treated with aversion therapy had significantly higher abstinence rates at six and twelve months. Patients who accepted a booster dose after one and three months showed better outcome than the others. The patients receiving CAT had greater job stability, were more likely to live with a relative, and had no criminal records compared with the comparison group, all factors that can improve outcome, suggesting that the comparison was confounded by differences on background characteristics.

Several early studies lacked control and comparison groups. Lemere and Voegtin (1940) reported the results of a study based on the follow up 10 to 15 years after treatment of more than 34,000 patients who were conditioned to feel nauseated when exposed to alcohol. Sixty-six percent of these patients were abstinent, an impressive recovery rate compared to other forms of treatment. The patients who were most successful had undergone booster sessions; that is, they had returned to the clinic after the initial treatment to repeat the conditioning procedure. Of those who attended booster sessions, 90 percent were abstinent.

Frawley and Smith (1992) also reported remarkably high rates of abstinence from cocaine (current abstinence of at least six months, 68%) among a similar group of patients with good prognostic features, treated with aversion therapy. These patients were followed up for an average of 15 months after treatment. Again there was no control group.

From the 1950s to the 1970s, CAT was offered in a large variety of settings in the United States. After that, the use of CAT diminished considerably, and only the Schick Shadel Hospital still offered the therapy in 2008.

In conclusion, the efficacy of CAT is not well documented. There have only been a few randomized controlled trials, and these lacked sufficient statistical power and had other methodological limitations, yielding inconclusive results. Adequate evaluations of the efficacy of CAT will require that clinical trials evaluating its efficacy use more rigorous clinical trial methods.

See also **Calcium Carbimide; Treatment, Pharmacological Approaches to: Disulfiram.**

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ACAMPROSATE

Acamprosate (brand name Campral) is a synthetic compound with a structure similar to that of the neurotransmitter gamma-aminobutyric acid (GABA) and the neuromodulator taurine. Not completely understood as of 2008, the mechanism of action in this drug was thought to involve a functional antagonism of the glutamate n-methyl-d-aspartate (NMDA) receptor, including antagonism of the mGLu5 metabotropic glutamate receptor, to counteract the imbalance between the glutamate and GABA systems associated with chronic alcohol exposure and alcohol withdrawal. This effect may reduce craving and distress and may thus decrease the need to consume alcohol.

In double-blind, placebo-controlled trials, acamprosate effectively maintained complete abstinence in detoxified alcohol-dependent patients at a rate significantly higher than an inactive placebo. When used as an adjunct to psychosocial interventions, acamprosate also improves the length and rate of abstinence from alcohol. This effect is less likely if acamprosate is not initiated quickly after detoxification.

As of 2008, however, the success of acamprosate had only been demonstrated in trials conducted in Europe. In a meta-analysis of 17 randomized controlled trials conducted in Europe, which included 4,087 recently detoxified alcohol-dependent patients receiving psychosocial support, treatment with acamprosate for six months resulted in significantly higher rates of continuous abstinence than placebo. In contrast, acamprosate did not show efficacy in two U.S. studies.

The multicenter COMBINE study included 1,383 recently alcohol-abstinent patients with alcohol dependence and compared the efficacy of medical management plus oral naltrexone or acamprosate with placebo, combined with an intensive behavioral therapy or a less intensive medical management procedure. COMBINE found that acamprosate was no better than placebo, failing to produce either a greater decrease in the rate of heavy-drinking days or a greater increase in abstinent days from that seen with placebo treatment.

In the second U.S. clinical trial, there was an effect for acamprosate compared with placebo only in a subset of highly motivated patients. The reasons for the differences in effectiveness of acamprosate between European and U.S. studies were unknown as of 2008. It was hypothesized that differences in features that characterize patients (e.g., concurrent drug abuse, which is more common in the U.S. population) and greater severity of alcoholism and the use of inpatient detoxification in European populations may help to explain these findings.

Acamprosate has been approved for use in Europe since 1989 and was approved by the U.S. Food and Drug Administration (FDA) in July 2004 for abstinence maintenance in alcohol-dependent individuals who are abstinent at treatment initiation. Acamprosate is dispensed in 333 mg white and odorless tablets of acamprosate calcium, which is equivalent to 300 mg of acamprosate. The usual dose is 666 mg (i.e., two tablets) three times daily. Acamprosate is not well absorbed into the blood from the digestive tract, and it takes several days to achieve desired blood levels of the medication. The medication appears to be safe in alcoholics, with minimal side effects. It does not appear to produce sedation and does not cause drug dependence.

The most common adverse effects of acamprosate are headache and gastrointestinal effects, including nausea, diarrhea, and bloating. Because it only has these benign side effects, the drug can be started at full dosage without needing to be gradually increased. Acamprosate is not metabolized but is eliminated by renal excretion. It should therefore be given cautiously to patients with impaired kidney function (creatinine clearance = 30mL/min). The drug should be avoided in patients who previously exhibited hypersensitivity to acamprosate.

See also **Alcohol: Chemistry and Pharmacology; Alcoholism: Abstinence versus Controlled Drinking; Drug Interactions and Alcohol.**

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BUPRENORPHINE

Buprenorphine is a semisynthetic opiate that is produced from thebaine, a naturally occurring alkaloid present in the ripe pods of the opium poppy (*Papaver somniferum*). Buprenorphine has an analgesic potency twenty-five to fifty times greater than morphine on a weight basis. However, after taking into consideration its greater potency, the analgesic actions of buprenorphine are quite similar to those of morphine and the other opiates, such as codeine, hydromorphone, oxymorphone, and fentanyl.

It is assumed that these effects are dependent upon its ability to act at *mu* (morphine) receptors in the brain. Once bound to the receptor, however, buprenorphine produces a limited effect, and thus it is termed a partial agonist. This ability to produce only a partial response may explain why buprenorphine has a lesser effect on reducing breathing (i.e., produces respiratory depression) than drugs such as morphine.

Because it is a partial agonist, buprenorphine administration to morphine-dependent patients does not elicit significant withdrawal symptoms and can therefore be used as a methadone-like opiate substitute in treatment programs. Another reason for the use of the agent in this respect is its particularly long duration of action. Single doses of buprenorphine can attenuate or prevent many of the actions of morphine for up to thirty hours. Thus, buprenorphine maintenance is used to treat opiate addiction.

The interactions of buprenorphine with opioid antagonists are interesting. Buprenorphine actions can be readily prevented by antagonists such as naloxone when the antagonist is administered prior to buprenorphine. However, antagonists given after buprenorphine do not readily reverse the opioid actions. This unique pharmacology distinguishes it from traditional opiates such as morphine. Many believe that this observation is due to the prolonged occupation of the receptor by buprenorphine. Once it is bound, other drugs can no longer effectively compete with buprenorphine to bind to the receptor.

Buprenorphine is available alone (Subutex) or in a 4:1 combination sublingual tablet with naloxone (Suboxone). A multi-center, randomized, placebo-controlled clinical experiment comparing buprenorphine tablets, Suboxone tablets, and placebos in opiate-dependent patients found that both buprenorphine alone and Suboxone reduced opiate use in the first month of the study compared to a placebo. Suboxone also appears to decrease the potential for abuse or diversion compared to methadone because injection of Suboxone can precipitate opioid withdrawal in an individual that is opiate dependent (due to the presence of naloxone, which is broken down before reaching the brain when taken orally). In 2002 the Food and Drug Administration (FDA) approved buprenorphine monotherapy (Subutex), as well as Suboxone, (the buprenorphine/naloxone combination product) for use in opioid addiction treatment. Subutex and Suboxone are currently the only Schedule III, IV, or V medications to have received FDA approval for this indication.

In addition, buprenorphine has been examined for use in HIV-infected patients with opioid dependence to improve treatment outcomes and to evaluate its role in HIV prevention. Following its initial approval, the drug has been made more widely accessible in healthcare settings by a law allowing individual physicians to treat up to 100 patients in private offices.

See also **Heroin; Treatment, Pharmacological Approaches to: An Overview.**

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CLONIDINE

While not itself life threatening, the opioid withdrawal syndrome is extremely unpleasant and contributes to further opioid use and relapse. Heroin addicts report that the acute withdrawal syndrome begins approximately eight hours after their last injection and includes the following: craving for the drug, anxiety, perspiration with hot and cold flashes, tearing of the eyes and runny nose, restlessness, problems falling asleep and poor sleep quality, goose bumps, aching bones and muscles, loss of appetite, nausea, vomiting, diarrhea, abdominal cramps, spontaneous yawning, and a group of flu-like symptoms.

Opiate activation of mu opioid receptors in brainstem noradrenergic nuclei, including the locus coeruleus (LC), the major noradrenergic nucleus, suppresses neuronal activity, cyclic adenosine monophosphate (cAMP) signaling pathways, and norepinephrine (NE) release. In response to the chronic suppression induced by opiates, homeostatic mechanisms within these nuclei compensate by upregulating a number of molecules, including tyrosine hydroxylase (the rate-limiting enzyme for NE synthesis), cAMP response element binding protein (CREB), and adenylate cyclase. Upon opiate withdrawal and the absence of mu opioid activation, the noradrenergic system is disinhibited and, in fact, becomes overactive due to the persistence of the compensatory changes that took place during chronic opiate exposure. This noradrenergic hyperactivity significantly contributes to the opiate withdrawal syndrome described above. Some studies have implicated noradrenergic nuclei outside the LC, such as the nucleus tractus solitarius (NTS), in the opiate withdrawal syndrome.

CLINICAL CLONIDINE USE FOR OPIATE WITHDRAWAL

In the late 1970s, Gold and coworkers proposed that the alpha-2 adrenergic receptor agonist and hypertensive drug clonidine could be an effective treatment for opiate withdrawal distress. The alpha-2 adrenergic receptor is expressed by noradrenergic neurons, where it functions primarily as an inhibitory autoreceptor. Because activation of alpha-2 autoreceptors suppresses noradrenergic neuron firing and NE release, it dampens the hyperactivity of noradrenergic neurons that occurs during opiate withdrawal.

Clonidine has been tried in numerous inpatient and outpatient opioid addict populations worldwide and studied by researchers in numerous well-controlled studies. In virtually all studies, clonidine has been shown to be a safe and effective non-opioid treatment that ameliorates several aspects of opioid withdrawal. Clonidine has its most demonstrable effects on autonomic elements of opioid withdrawal: sweating, gastrointestinal complaints (cramps, diarrhea, nausea), and elevated blood pressure. Direct infusion of clonidine into the LC or brain areas innervated by the NTS noradrenergic cell group in animals can attenuate some aspects of opiate withdrawal, implicating both central and peripheral actions of clonidine.

Traditionally, clonidine has been used for the treatments of adult opiate addicts. However, its use as a detoxification treatment has been extended to neonates born to opiate-dependent mothers and to adolescent addicts. Clonidine has also been used successfully as an adjunctive therapy with the opiate receptor antagonist naltrexone or the partial opiate receptor agonist buprenorphine. In some cases, clonidine plus naltrexone shortened the detoxification period compared to naltrexone alone. Rapid opioid detoxification (ROD) with opioid antagonist induction using general anesthesia has emerged as an alternative approach to treat opioid dependence, but its safety and efficacy were the subject of debate as of 2008. In randomized trials, the success of clonidine-assisted detoxification has been comparable to that of ROD, but without the life-threatening risks of ROD. Using clonidine for withdrawal distress allows the brain to reestablish normal

homeostatic patterns when given as part of a long-term recovery program. It allows patients sufficient motivation to achieve and sustain drug-free existence.

CLINICAL UTILITY OF CLONIDINE FOR OTHER ASPECTS OF DRUG ADDICTION

The noradrenergic system is involved in the processes underlying addiction to drug classes besides opiates, such as psychostimulants (e.g., cocaine, amphetamine), alcohol, and nicotine. Specifically, NE appears to be critical for the rewarding properties of morphine, ethanol, cocaine, and amphetamine. Although there are few clinical data to support it, clonidine may attenuate drug reward by acting on alpha-2 adrenergic autoreceptors and suppressing NE release.

It is widely agreed in the psychiatric community that stressful situations often precipitate relapse in abstinent drug-dependent individuals. Because the noradrenergic system is potently activated by stress, it has been hypothesized that blocking NE release (e.g., with clonidine) might attenuate stress-induced relapse. In the first decade of the twenty-first century, the stress-induced reinstatement paradigm gained popularity in rodents and nonhuman primates as a model for the stress-induced relapse observed in abstinent drug addicts. This paradigm consists of training animals to press a lever to obtain the drug, then extinguishing the lever pressing behavior by stopping drug delivery even upon correct lever presses. The lever pressing behavior can be reinstated by exposing the animal to various types of acute stress. Numerous studies have demonstrated that clonidine can block stress-induced reinstatement of heroin, cocaine, alcohol, and nicotine seeking in rats and monkeys. Its efficacy in preventing relapse in human addicts was unknown as of 2008.

CLINICAL UTILITY OF CLONIDINE FOR OTHER NEUROPSYCHIATRIC DISORDERS

Clonidine has been tried with varying success in the treatment of a number of medical problems in which the behaviors, signs, and/or symptoms resemble those seen in opiate withdrawal or following noradrenergic hyperactivity. Clonidine has also been tried in humans with generalized and panic anxiety, obsessive-compulsive symptomatology, Gilles de La Tourette's syndrome, mania, attention deficit and hyperactivity disorder, narcolepsy, neuroleptic-induced akathisia, and pheochromocytoma. Clonidine's analgesic effects have been rediscovered, and the drug has been given orally, transdermally (using skin patches), epidurally (into the area around the spinal canal), and parenterally (by injection) to decrease anesthetic requirements and to effect less respiratory depression than opioids alone.

Research and clinical experience since the original discoveries have (1) supported the notion of noradrenergic hyperactivity as one of the neural substrates for opioid withdrawal syndrome and led to considerable progress in the understanding of the critical cellular events causing noradrenergic hyperactivity in opioid withdrawal; (2) supported the efficacy of clonidine and established clonidine detoxification as one of the standard treatments for opioid addicts; (3) demonstrated that some individuals can receive further benefit from clonidine in combination with other drugs such as buprenorphine and naltrexone; and (4) suggested that clonidine may be useful for the treatment of other drug dependencies and neuropsychiatric diseases.

See also **Opioid Complications and Withdrawal.**

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DISULFIRAM

Disulfiram (Antabuse) was the first medication to be approved for alcoholism and for nearly fifty years was the only FDA-approved medication for alcoholism. Since 1994, three other medications were approved by the FDA for alcohol dependence treatment: oral naltrexone (ReVia), acamprosate (Campral), and long-acting intramuscular naltrexone (Vivitrol). The use of disulfiram has remained relatively constant and modest over the years. However, it may be anticipated that with the advent of subsequent medications that target the disease process of alcohol dependence more directly, the use of disulfiram may slowly wane. Disulfiram is not intended as a substitute for the counseling alcoholics receive while in treatment; it is meant to be an aid in keeping alcoholics sober, so that they may benefit from counseling. Although disulfiram has been in clinical use since the late 1940s, it is only since the 1980s that its efficacy has been studied using appropriate scientific methodology.

Disulfiram is used to deter drinking by causing an unpleasant reaction if a medicated person drinks alcohol (ethanol). This reaction is called the disulfiram-ethanol reaction (DER); the symptoms include flushing, dizziness, rapid heartbeat, nausea, vomiting, and headache. The DER can vary in severity, and the degree of severity often depends on the dose of disulfiram being taken plus the amount of alcohol that was consumed. A DER can cause hypotension (low blood pressure) and can be so severe that death occurs, although with adjusted dosage regimens this is very rare.

Disulfiram blocks the action of several of the body's enzymes, including aldehyde dehydrogenase (ALDH) and dopamine-β-hydroxylase. The inhibition of ALDH is responsible for the DER, which occurs because ethanol (drinking alcohol) is metabolized in the liver to acetaldehyde. Acetaldehyde, in turn, is converted to acetic acid, which is metabolized to water and carbon dioxide. Aldehyde dehydrogenase is the enzyme that facilitates the metabolism of acetaldehyde to acetic acid. When the action of ALDH is inhibited by disulfiram, acetaldehyde is not effectively converted to acetic acid but accumulates in the blood. Most of the symptoms of the DER are due to the increased circulating acetaldehyde. Since the inhibition of ALDH by disulfiram is irreversible, a person taking disulfiram cannot stop taking it one day and begin drinking the next: Several days (up to fourteen but usually fewer than seven) must go by because this amount of time is necessary for the body to produce new enzyme.

Attention has been drawn to positive findings with disulfiram in the management of cocaine dependence (Carroll et al., 2004). These effects are independent of an effect on alcohol consumption and have been hypothesized to relate to other biological actions of disulfiram such as its inhibition of dopamine-β-hydroxylase. This latter action likely affects the dopaminergic/noradrenergic transmission in the brain, which likely plays a role in cocaine addiction.

OTHER MEDICATIONS

Certain other medications cause a mild DER, including the antibiotic metronidazole (Flagyl). A medication available in Canada but not in the United States as of 2008 is citrated calcium carbimide (Temposil), which inhibits ALDH in a mixed reversible-irreversible fashion. When citrated calcium carbimide is discontinued, 80 percent of ALDH activity is restored within 24 hours. Hence, one can drink alcohol as soon as a day after stopping the use of citrated calcium carbimide without having a reaction.

In addition to disulfiram, there are medications with different mechanisms of action that are approved for use as of 2008 in helping recovering alcoholics maintain sobriety or reduce destructive drinking behavior. Oral naltrexone hydrochloride (ReVia) and long-acting intramuscular naltrexone (Vivitrol) are opioid antagonists that block the effects of endogenous opioids such as β-endorphin that are released by alcohol. The blockade of opioids counteracts the high feeling after alcohol consumption, and these medications have been found to reduce heavy drinking rates, to reduce relapse to heavy drinking, and, to some extent, enhance abstinence. Acamprosate (Campral), another medication approved for alcoholism, is thought to work by counteracting hyperglutamatergic activity that likely occurs in the recovery phase from alcohol dependence. This action may reduce the protracted withdrawal syndrome thereby decreasing one factor that contributes to relapse. Acamprosate has been shown to enhance the likelihood of abstinence and to reduce the number of drinking days in patients who are receiving alcoholism treatment.

ADMINISTRATION AND DOSAGE

Disulfiram should be administered only by a physician and is given by mouth in tablet form. It should never be given until the patient has abstained from alcohol for at least twelve hours and preferably for forty-eight hours. The FDA-approved dosage is 250 mg daily. Some patients report not experiencing a DER with smaller doses, so larger doses may be required. Clinical experience indicates, however, that doses larger than 500 mg are accompanied by a greater risk of serious side effects. A problem that limits the effectiveness of disulfiram is that patients frequently stop taking the medication. To enhance compliance, supervised administration by either a family member, treatment program, or even the legal system should be considered. Supervised administration has been shown to enhance outcomes in some trials (Chick et al., 1992; Martin et al., 2003). Given that compliance is perhaps the most significant impediment to the effective use of disulfiram, the development of a long-acting formulation of disulfiram has been a goal of research for many years. Unfortunately, no depot formulation of disulfiram has been developed, so clinicians and patients are left to use only oral disulfiram.

Patients should take disulfiram only under careful medical supervision. They should be warned that as long as they are taking the drug, ingesting alcohol in any form will make them sick and may be life-threatening. Patients should be taught to recognize and avoid disguised forms of alcohol such as cough syrups, mouthwashes, some sauces, fermented vinegar, and even aftershave lotion or rubbing alcohol. In addition, patients should be taught to recognize the signs of disturbed liver function (jaundiced eyeballs or skin, nausea or pain in the upper right quadrant of the abdomen, dark urine, clay-colored stool) and report them at once to their doctor. Patients should also be warned about signs of peripheral neuropathy, including sensory changes or weakness in the hands or feet.

SIDE EFFECTS

The use of disulfiram may be accompanied by side effects. The most common one is drowsiness; for this reason, the medication is usually taken at bedtime. Timing is usually sufficient to take care of this problem, but if not, the medication may have to be discontinued, especially for those who drive or work in hazardous environments. Idiosyncratic liver toxicity can occur from taking disulfiram. For this reason, liver function must be monitored

closely during the first several months of treatment, and if blood tests indicate possible liver damage, disulfiram must be discontinued immediately.

A 1986 Swedish study found that disulfiram enhances the absorption and toxicity of lead in rats. Recovering alcoholics who must work in environments containing lead or lead products are advised not to use disulfiram to maintain sobriety.

In addition, serious psychotic reactions and depressive episodes have occurred in patients taking disulfiram. In a multisite study of 605 men, admissions for psychiatric problems were uncommon; as many admissions of this type occurred in men taking the placebo or not receiving disulfiram as in those receiving a 250-milligram dose (Branchey et al., 1987). The risk of serious psychoses or of major affective illnesses appears to be greater with higher doses.

Disulfiram has also been associated with cases of peripheral neuropathy. Patients should be cautioned to alert their physician if they note changes in sensation or weakness in the hands or feet.

INTERACTIONS WITH OTHER DRUGS

Disulfiram should not be given to patients who are taking metronidazole (Flagyl), which can also cause a reaction similar to disulfiram when combined with alcohol or paraldehyde (Paral). Doing so can produce a reaction similar to the DER. Amprenavir oral solution is contraindicated because it contains high levels of propylene glycol, which is also metabolized by aldehyde dehydrogenase, so that patients administered disulfiram could develop toxic levels of propylene glycol. Patients taking isoniazid (INH, Laniazid) may develop neurological symptoms if given disulfiram. Lastly, disulfiram may increase the blood levels and toxicity of warfarin (Coumadin), barbiturates, and phenytoin (Dilantin).

See also **Naltrexone; Relapse; Treatment: An Overview of Alcohol Abuse/Dependence.**

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LONG-ACTING PREPARATIONS

Poor medication compliance is a significant problem in clinical medicine (Osterberg & Blaschke, 2005), including adversely affecting the medical management of substance use disorders. One approach to dealing with compliance problems is to use long-acting preparations of medications. Early efforts to develop a long-acting formulation of disulfiram (Antabuse) for alcohol dependence were unsuccessful (Garbutt et al., 1999). However, subsequent efforts to develop a long-acting preparation of naltrexone were much more successful. Several clinical trials were completed as of 2008, demonstrating the efficacy and safety of long-acting naltrexone formulations (LA-NTX) for the treatment of alcohol dependence (Garbutt et al., 2005; Kranzler et al., 2004). In alcohol dependent patients, LA-NTX was effective in reducing rates of heavy drinking, and they

enhanced rates of total abstinence (Garbutt et al., 2005; Kranzler et al., 2004; O'Malley et al., 2007). Early evidence supported the efficacy of LA-NTX in opioid dependence as well (Comer et al., 2006), but additional work was required to verify this finding. As of 2008, LA-NTX was approved by the U.S. Food and Drug Administration (FDA) only for the treatment of alcohol dependence.

Naltrexone blocks endogenous opioid receptors thereby counteracting the effects of opioids released by alcohol. This action in turn counteracts the *high* experienced when alcohol is consumed and reduces the risk for relapse to heavy drinking. Naltrexone also blocks the effects of opioid drugs such as heroin or oxycodone. A patient taking oral or LA-NTX naltrexone will not experience the *high* from taking an opioid drug and, therefore, has a markedly reduced behavioral incentive to use opioid drugs.

Several LA-NTX formulations have been developed and studied in moderate-to-large clinical trials for alcohol dependence (Kranzler et al., 2004 [n=315]; Garbutt et al., 2005 [n=624]) and in a smaller trial in opioid dependence (Comer et al., 2006 [n=60]). These formulations use a polylactide polymer base, similar to that used in absorbable sutures, to provide a slow-dissolving matrix in which naltrexone is imbedded. This methodology has been shown to yield adequate levels of naltrexone for 28 days after injection (Johnson et al., 2004; Kranzler et al., 1998).

The one approved formulation of LA-NTX is for the treatment of alcohol dependence. It is given as a single, 380 mg, deep intramuscular injection in the buttock. It is recommended that the injection site be alternated from one buttock to the other. Injections are given once a month. The FDA label recommends that LA-NTX be started in patients who are able to abstain from alcohol in an outpatient setting prior to the initiation of treatment. The length of administration is not well defined. Most clinicians recommend that LA-NTX be used for 6 to 12 months together with counseling. Patients who have acute hepatitis or liver failure or who are abusing opiates or taking opiates for medical reasons should not receive LA-NTX.

LA-NTX has been associated with a number of side effects. Injection site reactions include tenderness, swelling, and pain and are common (69%), though usually well tolerated. Nausea is also common (33%) though generally short-lived. Other side effects include vomiting (14%), abdominal pain (11%), insomnia (12%), and anxiety (14%).

The primary drug-drug interaction with LA-NTX is with opiates such as oxycodone or morphine. Opiates will not have their expected pharmacological effect in the presence of naltrexone. Furthermore, opiate blockade can present a problem when a patient needs opiate treatment for acute pain. For acute pain conditions it is recommended that non-opiate interventions such as non-steroidal analgesics and regional analgesia be used. In cases in which opiates are necessary, high potency agents may be needed to override the blockade and, given the potential for adverse effects of such an override, should be monitored carefully. No other prominent drug interactions have been reported.

See also **Naltrexone.**

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METHADONE

Methadone (Dolophine) has pharmacological actions similar to those of the opioid drug, morphine. Methadone serves an important place in the history of opioid analgesics, since it is one of the first synthetic agents (having been synthesized in 1939). The ability to synthesize opioid analgesics from simple chemicals diminishes people's reliance on natural products (such as morphine, codeine, and thebaine) to provide the base for many opioid analgesics commonly used in the 2000s. Structurally, the drug does not look like morphine. Unlike the rigid fused ring structures of morphine, the structure of methadone is extremely flexible. It bends so that the key portions of the molecule can assume positions similar to those of morphine. The structure of methadone is similar to that of propoxyphene (Darvon), a weaker opiate widely used to treat mild-to-moderate pain. It has two stereoisomers, but the (-)isomer is far more active than the (+)isomer. Methadone can be administered orally, intramuscularly, or intravenously. It is well absorbed from the gastrointestinal tract making it useful orally. Its oral/parenteral ratio of potency is approximately two, far better than many other opioids. Methadone is threefold more potent than morphine orally, but about equipotent when given by injection. It is metabolized by the liver to a variety of inactive compounds, which then are eliminated by the kidneys.

Pharmacologically, methadone is used in the form of its hydrochloride salt. It has actions quite similar to morphine and works predominantly through mu opiate receptors. Like all mu opioid drugs, methadone elicits a variety of side effects, including respiratory depression, sedation, and constipation, in addition to pain relief. Although their potency is similar, the long half-life of methadone distinguishes it from morphine. For pain control, the drug is typically given to patients every six to eight hours. This long duration of action can be advantageous, particularly in patients who require the drug for long periods of time, such as cancer patients.

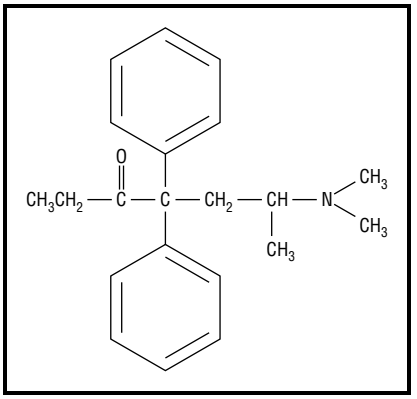

Figure 1. Chemical structure of methadone. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

However, there are some disadvantages. With a half-life ranging from twenty to thirty hours, it may take many days of continued dosing to reach constant (or steady-state) levels of the drug in the body. Thus, the full effect of a change in drug dose may not be seen for three or four days. This factor may make it difficult to adjust the dose for an individual patient. Increasing the dose too rapidly may even lead to delayed increases in its concentration in the body, far beyond those anticipated and, in some situations, may actually lead to an overdose. Continued administration of methadone will produce tolerance and physical dependence. The actions of methadone, like those of morphine, are readily reversed by antagonists such as naloxone or naltrexone; however, these antagonists will also produce an immediate withdrawal syndrome in physically dependent people. Despite its clear utility in the control of pain, the major use of methadone in the United States is in the treatment of heroin addicts. Although methadone must be administered approximately every six to eight hours to maintain analgesia, its slow rate of elimination prevents the appearance of withdrawal signs and symptoms for over twenty-four hours. This slow appearance of withdrawal effects has made this

agent useful in maintenance programs, since it permits once-a-day dosing. With chronic administration of high doses of methadone, addicts become tolerant, markedly limiting the euphoria an addict might obtain from illicit use of other opiates such as heroin. Thus, methadone minimizes occasional opiate use, is readily tolerated by the addicts, and can be administered once a day, which makes it easily dispensed. Methadone has been used clinically in maintenance programs and is one of the most effective treatment modalities as of 2008 available for opiate addicts.

See also **Addiction: Concepts and Definitions; Methadone Maintenance Programs; Pain, Drugs Used for; Treatment, Pharmacological Approaches to: An Overview.**

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NALTREXONE

Naltrexone (Depade, Revia Vivitrol [U.S.]; Nalorex [France, U.K.]) is a synthetic antagonist of opioid (morphine-like) receptors, which blocks their actions without having any opioid effects itself. Naltrexone differs from most other pure opioid antagonists in having a relatively long duration of action (at least twenty-four hours) and being effective when taken by mouth or as a depot formulation (long-acting injection lasting thirty days). These characteristics have led to its clinical use as a long-term or maintenance treatment for alcohol and opioid dependence. As of 2008, Naltrexone was also being studied experimentally as a possible treatment for cigarette smoking.

OPIOID DEPENDENCE

The use of opioid antagonists as treatment for opioid dependence was first proposed by William Martin and Abraham Wikler and their colleagues at the U.S. Addiction Research Center in the early 1960s. These researchers hypothesized that chronic administration of an opioid antagonist, by blocking the pleasurable or rewarding effects of opioid drugs, would lead to the extinction of drug-seeking and drug-taking behavior—since the addict would no longer receive any pleasurable effects from taking an opioid. It was further suggested that antagonist treatment would have several advantages over treatment with an opioid such as methadone. Since antagonists do not produce any pleasurable effects, addicts have little incentive to misuse the medication or divert it to illegal channels. Chronic use of an antagonist would not produce physical dependence, and an overdose of antagonist would not cause life-threatening opioid effects such as suppression of breathing. Use of the antagonist in non-detoxified opioid addicts, however, would cause an acute but not life-threatening withdrawal reaction.

ALCOHOL DEPENDENCE

The efficacy of naltrexone for the treatment of alcohol dependence was established in at least twenty-three placebo-controlled randomized clinical trials, with many fewer trials failing to show a significant between-groups difference. The demonstration that naltrexone is effective in the treatment of alcohol dependence followed many years of human and animal research, which investigated the role of the opioid system in mediating the response to pain and pleasure. In December 1994, the FDA approved naltrexone, the first new medication for alcohol dependence in nearly 50 years, to be used in conjunction with psychosocial support to treat alcohol dependence. Research demonstrated that when used in conjunction with a psychosocial treatment program, naltrexone results in better treatment outcomes, particularly reducing the risk of relapse to heavy drinking. The mechanism of action is theorized to be a reduction in craving or alcohol stimulation effects such that when alcohol is consumed in the presence of naltrexone, the individual does not report as much reward and thus does not drink heavily.

TREATMENT

Opioid Dependence. Naltrexone is usually used in conjunction with counseling and other rehabilitation services, as part of a structured and

monitored treatment program. The best treatment results tend to occur in highly motivated, psychologically healthy individuals who are employed and well-functioning socially, especially when they face severe economic or legal consequences for failing treatment. For example, addicted health professionals whose treatment is required by their professional licensing boards and monitored as a condition of continued licensure will regularly take naltrexone for several years and remain abstinent from opioids. Some programs have reported five-year success rates as high as 95 percent. Most street addicts (e.g., those with unstable living situations who support their drug use by criminal activity) refuse to take naltrexone or, if started in treatment, quickly drop out. This pattern is believed to be due to the lack of rewarding effects and the blockade of such effects when opioid drugs are self-administered. Many such addicts prefer maintenance treatment with the synthetic opioid methadone, and others find even methadone non-rewarding, so they relapse. Use of the depot formulation of naltrexone for opioid addiction was not FDA approved as of 2008 but may provide an alternative to methadone and assure treatment adherence for at least thirty days.

Fifty mg of naltrexone blocks the effects of 25 mg of heroin for twenty-four hours, so the typical weekly naltrexone dose for the treatment of opioid dependence is 350 mg. The actual medication schedule is adjusted to the individual patient and may range from 50 mg every day to 150 mg every third day. Patients are put on the least frequent medication schedule possible to enhance patient cooperation and reduce the number of clinic visits. The use of long-acting naltrexone in the treatment of opioid dependence, which can be injected once a month and which slowly releases the medication into the body, could substantially reduce the frequency of required visits but is not FDA approved for use in opioid addiction as of 2008.

Care must be taken to avoid administering naltrexone to individuals still physically dependent on opioids. In opioid-dependent individuals, an antagonist will precipitate an acute opioid withdrawal syndrome. While not life-threatening, this syndrome can be extremely uncomfortable, with symptoms such as abdominal cramps; diarrhea; muscle, joint, and bone pain; runny nose (rhinorrhea); and goose bumps (piloerection). To avoid this situation, naltrexone is not administered to patients until they have been free of opioid drugs for at least seven to ten days to allow dependence to wear off. To confirm the absence of dependence, patients may be challenged with the short-acting antagonist naloxone before starting on naltrexone.

Alcohol Dependence. Again naltrexone or any other addiction pharmacotherapy should be given in conjunction with appropriate counseling or participation in an addiction treatment program. Ideally, naltrexone is started after two to three days of abstinence but can be used even when patients continue to drink. Abstinence may reduce the chance of side effects and establishes a level of motivation for treatment. Patients with severe liver disease should not take naltrexone unless under very close monitoring. The usual starting dose is 50 mg per day for the oral medication although a starting dosage of 25 mg may reduce the chances of side effects. Doses between 25 and 150 mg have been used in treatment, though generally 50 or 100 mg provides sufficient coverage. The depot formulation has been shown to be effective in reducing heavy drinking among alcohol dependent individuals and has the advantage of providing thirty days of treatment coverage. Some studies have suggested patients with a family history of addiction or possibly with a specific genotype may be the most responsive to treatment. As with the treatment of opioid addiction, care must be taken to avoid treatment in patients currently taking an opioid either abusively or by prescription. Most studies have found that reduction in heavy drinking (bingeing) is the major beneficial effect of naltrexone treatment though some research also shows that the medication improved the rate of abstinence.

See also **Treatment: An Overview.**

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SEROTONIN-UPTAKE INHIBITORS

Successful pharmacotherapy of substance-related disorders requires an understanding of the factors that contribute to the development and maintenance of drug-seeking behaviors. Within this framework, insight into the neurochemical basis for drug addiction and the workings of the brain's reward circuit is key. Preclinical studies have demonstrated the importance of the neurotransmitters serotonin and dopamine in mediating the rewarding effect of substance use. Drugs that increase serotonergic neurotransmission have, therefore, been studied as treatments for abuse of a variety of substances. Serotonin uptake inhibitors, which are generally marketed as antidepressants, block the reabsorption of serotonin and increase its concentration in the nerve synapse. As of the first decade of the twenty-first century, they show some promise as effective treatments for the abuse of alcohol and other drugs.

Additionally, substance abuse or dependence often co-occurs with psychiatric disorders, including depression and anxiety, and patients who have both a substance use disorder and a psychiatric disorder are, in general, more difficult to treat successfully. The cause-and-effect relationships are unclear: Researchers seek to know if depressed and anxious patients self-medicate with drugs and alcohol or if anxiety and depression are consequences of addiction. In any given patient, both are likely true to some degree. As many serotonin uptake inhibitors are indicated for the treatment of anxiety and depression, it stands to reason that they may be especially useful in patients who have both addiction and anxiety or depression.

ALCOHOL

Clinical and preclinical research since the 1980s has demonstrated an inverse relationship between serotonergic activity and alcohol use. However, evidence available as of 2008 suggests that serotonin uptake inhibitors are not consistently effective as treatment for alcohol abuse or dependence in heterogeneous groups. They do show promise in specific groups of alcoholics, including specific genetic groups, early- or late-onset alcoholics, and alcoholics with comorbid anxiety or depression. Some evidence suggests that there may be distinct subtypes of alcoholism that may be distinguishable by the type and complexity of the serotonergic dysfunction. Response to serotonin uptake inhibitors varies greatly by individual, with drinking reductions from 10 to 70 percent in some studies. A major challenge is predicting which patients will respond to treatment.

A 2004 study showed that lower risk/lower severity alcoholics showed a better response to sertraline, as measured by time to relapse, days drinking, days drinking heavily, drinks per drinking day, and number of participants who were continually abstinent. These gains were consistent out to six months after treatment ended. Similar to findings of a previous study on citalopram, this study found that among these lower risk/lower severity alcoholics, men responded to sertraline better than women did, with women failing to show a difference from placebo on several measures. This difference was not found in the higher risk/higher severity alcoholics. This study, when analyzed using a different approach, showed that sertraline was superior to placebo in reducing drinking in alcohol dependent patients with no personal or family history of depression but was no better than placebo in patients with a personal history of depression—a somewhat counterintuitive result. A large study of sertraline for treatment of co-occurring alcohol dependence and major depression showed no advantage of the serotonin uptake inhibitor compared with placebo, either on measures of drinking or depressive symptoms. It seems clear that studies are needed to determine which subtypes of alcohol

abuse and dependence are most responsive to treatment with serotonin uptake inhibitors.

COCAINE

Cocaine is a common drug of abuse and is used in a variety of ways—by smoking, snorting, or injection. As of 2008, there were no FDA-approved drugs for the treatment of cocaine addiction. Preclinical studies suggested that serotonin plays an important role in the dopamine reward pathway that is activated by cocaine use, suggesting a possible role for serotonin uptake inhibitors in the treatment of cocaine dependence. A randomized, double blind, placebo-controlled study done in 2007 showed that citalopram was more effective than placebo in reducing the number of cocaine-positive urines in patients also being treated with cognitive-behavioral therapy and contingency management. However, similar studies with sertraline, paroxetine, and venlafaxine failed to show an effect.

OPIATES

Opiate addiction is most commonly treated with opiate-agonist therapy, such as methadone; however, treatment response is often incomplete. As of 2008, few studies of serotonin uptake inhibitors as treatment for opiate dependence had been conducted in humans. A 2007 study failed to show an effect of citalopram as compared to placebo as adjunct for methadone maintenance therapy. A 2002 study showed that sertraline was not effective as an adjunct to naltrexone treatment. Fluoxetine was shown to decrease the dropout rate in a naltrexone treatment program for heroin dependence, but it did not show a specific effect on opiate use.

NICOTINE

Nicotine is an extremely common drug of abuse with multiple and severe negative health effects. Several therapies exist for treatment of nicotine dependence, including nicotine replacement therapy, bupropion, and varenicline. A 2004 study indicated that fluoxetine eases nicotine withdrawal symptoms, including weight gain, but did not reduce smoking. A 2007 study showed that paroxetine was effective, as compared to placebo, in reducing cigarette smoking in patients with major depression.

Serotonin uptake inhibitors show promise for some role in the treatment of substance use disorders. Evidence suggests that they are effective in particular subtypes of alcohol dependence, and studies with cocaine and nicotine, though few in number, show promise. As of 2008, there was little evidence that serotonin uptake inhibitors are an effective treatment for opiate dependence, although they may have a role in increasing treatment attendance.

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VACCINES

Drug addiction, broadly defined as a chronic relapsing illness, is characterized by compulsive drug-taking behavior resulting in impairment in social and occupational functioning (Koob & Kreek, 2007; Le Moal & Koob, 2007). The search for effective treatments has intensified recently due to a better understanding of the underlying neurobiological mechanisms contributing to drug use and relapse (Koob & Kreek, 2007; Volman, 2007; George et al., 2007).

Immunologic therapies have emerged recently as possible treatment options for drug dependence. Immunopharmacotherapy is based on the generation or administration of antibodies that are capable of binding the targeted drug before it can reach the brain. Pharmacological strategies based on agonists or antagonists of these drugs generally cause many undesired side effects and have yielded only limited success (Karila et al., 2008; Elkashef et al., 2007). A large amount of data has been gathered in recent years on the effects of active and passive immunization against cocaine, nicotine, phencyclidine (PCP), and methamphetamine in animal models, suggesting potential efficacy of these treatments in humans (Morland, 2006; Roiko et al., 2008; Orson et al., 2007; Kosten & Owens, 2005). However, these vaccines may not provide adequate protection against drug abuse in all individuals. For example, in a Phase II study of a cocaine conjugate vaccine with cholera toxin B (CTB) as the carrier protein only 30 percent of the subjects produced enough antibody to block the drug (Kosten & Singh, unpublished work), therefore improving the quantity and quality of IgG (a type of antibody) response to such vaccines, which is critical for their future success.

Some reports suggest that the immune system in a drug abuser is defective, which may explain the limited success of some vaccines (Cabral, 2006; Kelschenbach et al., 2008). Therefore, it is logical to investigate immunoregulatory cells and pathways involved in inducing humoral immune responses (i.e., those involving antibodies) for possible defects and to maximize their potential in upregulating the humoral immune response. It remains to be investigated whether antigen-presenting cells such as dendritic cell (DCs) populations and their functions in terms of signaling pathways/molecules are intact or defective in drug abusers. If the hypothesized defects are borne out, then an important question surfaces about whether their activities could be restored or maximized by using appropriate stimulatory agents or genetic vaccines.

The activities of helper and regulatory T cells are crucial for antibody production. Investigation into the role of these cell types in antidrug vaccination strategies warrants serious consideration and they should be exploited to enhance antibody production. The central aspect in all these vaccination strategies is B cells. It would be beneficial to devise strategies to produce long-lived hapten-specific plasma B cells and memory B cells. Furthermore, longevity of the specific antibodies for the abused substance is critically important. The formed antibodies should have a maximal half life to block the pharmacological activity of the drug for prolonged periods.

See also **Research, Animal Model: An Overview.**

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TREATMENT, SPECIALTY APPROACHES TO

This entry includes the following essays:

ACUPUNCTURE

The art of acupuncture is an ancient and integral part of the armamentarium that has been used in China for the treatment of medical problems for more than 2,000 years. Acupuncture consists of inserting very fine needles into the skin at specific points intended to, according to traditional Chinese medicine, influence specific bodily functions or body parts. In the traditional Chinese view of the body, life energy (chi) circulates through pathways; blockage of the pathways leads to a deficiency of chi, or disease. The goal of the traditional acupuncturist is to open up the pathways and stimulate the movement of chi. The specific points for needle insertion are based on traditional anatomical maps that depict which pathways affect which bodily functions.

HISTORY OF ACUPUNCTURE IN THE UNITED STATES

Following the historic trip to China in 1972 of U.S. president Richard M. Nixon, considerable public interest in acupuncture was generated when news coverage showed that acupuncture was effective not only in relieving pain, but also in substituting for general anesthesia. The following year, H. L. Wen, a neurosurgeon in Hong Kong, reported a serendipitous observation that acupuncture with electrical stimulation (AES) eliminated withdrawal symptoms in a narcotics addict for whom Wen had intended to perform brain surgery to treat drug addiction. Four needles were inserted into the right hand (at the defined points IL-4 and SI-3) and in the arm (EH-4 and TB-9), and another two needles were inserted into the right ear (brainstem and shen men). Fifteen minutes after AES began, the patient reported a significant reduction in drug withdrawal symptoms, which disappeared altogether 30 minutes after AES was started. Notably, Wen's initial observations occurred prior to the discovery in 1975 of endogenous opioid substances in the brain (also called endorphins).

In a 1977 study, Wen noted that AES increased endorphin levels and relieved abstinence syndromes while simultaneously inhibiting the autonomic nervous system, primarily the parasympathetic nervous system. The findings by Wen and several other scientific groups that peripheral stimulation could release endogenous opioids in the central nervous

system gave scientific credibility to the possibility that this traditional Chinese therapy could help to ameliorate a contemporary problem. Chronic or repeated exposure to opioids leads to adaptive changes in the central nervous system. Withdrawal symptoms occur when these drugs are abruptly discontinued. Because the administration of opioid drugs alleviates withdrawal, a reasonable hypothesis was that one's own endogenous opioids might do the same.

In 1985, Michael O. Smith founded the National Acupuncture Detoxification Association (NADA). Smith was interested in alternatives to methadone for detoxification. Based on Wen's work, Smith first used electrical stimulation together with acupuncture, but he later discarded the use of electrical stimulation. Eventually, a standard protocol was developed that used four or five acupuncture points on each ear. The NADA protocol of five treatment points is still regarded as the standard approach for this application.

In the early 1990s, the use of acupuncture in addiction treatment became popular with many people working in the criminal justice system. Most funding for treatment programs using acupuncture at that time came initially from the criminal justice system, rather than from the federal and state agencies that usually fund drug treatment programs. Although it should be emphasized that the scientific community has been unable to show the efficacy of acupuncture in properly controlled clinical studies, this relatively inexpensive and easily expanded procedure became the mainstay for a number of *drug courts*, where judges involved themselves directly in managing the treatment of drug offenders. Thus, as of 2008, it remained a popular approach, although scientific support for its effectiveness as a treatment for substance use disorders was lacking.

TECHNICAL PROCEDURES AND REVIEWS

As practiced in the United States, several technical procedures broadly described as acupuncture have been used. Standard bilateral acupuncture is the application of five needles to the concha and cartilage ridge of each ear at defined points (shen men, lung, sympathetic, kidney, and liver) determined from traditional Chinese anatomy maps. With unilateral acupuncture, the needles are applied to one ear. Acupressure involves applying pressure by hand or by an object to the same areas. Electroacupuncture applies low-level electric current to needles placed at the traditional points. With moxibustion, herbs are burned near the needles to add heat. With neuroelectric stimulation, low-dose electrical current is passed through surface electrodes. Some practitioners advocate the use of surface electrodes and special currents, designating this approach neuroelectrical therapy.

Many acupuncture practitioners in the United States belong to and are accredited by the American Association of Acupuncture and Oriental Medicine (AAAOM), founded in 1981. Others may be accredited by the National Acupuncture and Oriental Medicine Alliance (NAOMA), founded in 1992, which accepts a broader range of training than AAAOM does for purposes of certification.

In 1991, the National Institute on Drug Abuse (NIDA) sponsored a technical review of the current state of knowledge about the use of acupuncture in the treatment of alcoholism and other drug-dependence problems. One of the participants, George Ulett, noted that although there is some evidence that electrical stimulation through needles or electrodes placed at certain points on the body can release endogenous opioids and other neuropeptides in the central nervous system, little evidence exists that such opioid release is caused by the needles alone. Ulett asserted that a critical factor is the frequency characteristic of the current, not the specific placement site of needles or electrodes. This group of researchers concluded that part of the difficulty in deciding whether acupuncture is effective is the lack of standard terminology and standard methods.

A number of procedures, all called acupuncture, were being applied to a variety of drug and alcohol problems, but in different ways, over varying periods of time, with results measured in different ways. One study of acupuncture for alcohol detoxification, by Bullock and coworkers (1989), which came closest to being scientifically valid, used appropriate controls (i.e., placement of needles in non-specific sites) and staff who were blinded to which group was control and which group received acupuncture at specific bodily sites. This study found a far better outcome for patients in the specific body-site group than for controls.

The study also found that the difference persisted even when measured six months later. However, another research group using similar methodology could not replicate the findings and reported no difference between point-specific acupuncture, sham transdermal stimulation, or standard care (no acupuncture control) (Margolin et al., 2002). Further, Bullock and coworkers (2002) were unable to replicate their positive findings in a subsequent multi-center trial.

Many practitioners who have used acupuncture, even those who are convinced of its efficacy, report that only a small proportion of people who start treatment actually complete the typical series of ten to twenty treatments. Those who have used the technique believe that the minimal amount of treatment required for benefit is at least one twenty-minute session per day of bilateral acupuncture for at least ten days. In general, among both opioid-dependent and cocaine-dependent patients, those who have less severe dependence seem to fare the best.

The NIDA technical review panel concluded at the time of review in 1991 that no compelling evidence existed that acupuncture is an effective treatment for opiate or cocaine dependence. Nevertheless, they found no evidence that acupuncture is harmful. A major multi-site trial of acupuncture treatment for cocaine dependence found no evidence to support its effectiveness (Margolin et al., 2002).

See also **Cocaine; Drug Courts; Opiates/Opioids; Treatment, Stages/Phases of: Non-Medical Detoxification; U.S. Government Agencies: National Institute on Drug Abuse (NIDA).**

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HYPNOSIS

Hypnosis is a normal state of attentive, focused concentration with a relative suspension of peripheral awareness, a shift in attention mechanisms in the direction of focus at the expense of the periphery. Being hypnotized is something like looking through a telephoto lens. What is seen, is seen in great detail, but at the expense of context. The use of hypnosis has been associated with inducing a state of relaxation and comfort, with enhanced ability to attend to a therapeutic task, with the capacity to reduce pain and anxiety, and with heightened control over somatic function. For these reasons, hypnosis has been used with some benefit as an adjunct to the treatment of certain kinds of drug and alcohol abuse and addiction.

Therapeutic approaches involving hypnosis include using it as a substitute for the pleasure-inducing substance, taking a few minutes to induce a self-hypnotic state of relaxation (for example, by imaging oneself floating in a bathtub or a lake, or visualizing pleasant surroundings on an imaginary screen). In this strategy the hypnosis is a safe substitute for the pleasure-inducing effects of the drug. A second approach involves ego-enhancing techniques, providing the subject with encouragement, picturing himself or herself living well without the

substance, and able to control the desire for it. A third approach involves instructing subjects to reduce or eliminate their craving for the drug. A fourth involves cognitive restructuring, diminishing the importance of the craving for the drug by focusing instead on a commitment to respect and protect the body by eliminating the damaging drug. One widely used technique for smoking control, for example, has people in hypnosis repeat to themselves three points: (1) For my body, smoking is a poison; (2) I need my body to live; (3) I owe my body respect and protection. This approach places an emphasis on a positive commitment to what the person is for, rather than paying attention to being against the drug, thereby keeping attention on protection rather than on abstinence.

Hypnosis has been most widely used in the treatment of nicotine dependence, and although the results vary, a number of large-scale studies indicate that even a single session of training in self-hypnosis can result in complete abstinence of six months or more by approximately one out of four smokers.

There are fewer systematic data regarding use of hypnosis with cocaine, opiate, or alcohol addiction. The success of the approach is complicated by the fact that the acute effects of substance intoxication and/or the chronic effects on cognitive function of alcohol and other drug abuse hampers hypnotic responsiveness, thereby diminishing the potential of addicted individuals to enter this state and benefit from it. Nonetheless, there may be occasional individuals who are sufficiently hypnotizable and motivated to use this approach as an adjunct to other treatment, diminishing the dysphoria and discomfort that can accompany withdrawal and abstinence while enhancing and supporting their commitment to a behavior change. Hypnosis can be used by licensed and trained physicians, psychologists, dentists, and other health-care professionals who have special training in its use. The treatment is employed in offices and clinics as well as in hospital settings. It should always be used as an adjunct to a broader treatment strategy.

Hypnosis is a naturally occurring mental state that can be tapped in a matter of seconds and mobilized as a means of enhancing control over behavior, as well as the effects of withdrawal and abstinence, in motivated patients supervised by appropriately trained professionals.

See also **Nicotine; Withdrawal.**

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ADOLESCENTS

Adolescent substance use is a significant public health problem in the United States. Data from the national *Youth Risk Behavior Survey* indicate that between 2004 and 2006, 43 percent of high school students reported having at least one drink of alcohol and 26 percent acknowledged one or more instances of heavy drinking (defined as consuming five or more drinks in a row) during the previous thirty days (Centers for Disease Control and Prevention, 2006). Similarly, among a large national sample of twelfth graders participating in the *2007 Monitoring the Future* study, 36 percent reported using an illicit drug during the past year (Johnston, O'Malley, Bachman, & Schulenberg, 2008). The most commonly used drugs were marijuana (32%),

amphetamines (8%), sedatives (6%), hallucinogens (5%), cocaine (5%), and heroin (1%).

RISK FACTORS

Risk factors for adolescent substance use are well documented and involve influences at multiple individual and environmental levels (Schinke, Brounstein, & Gardner, 2002). At the individual level, adolescent substance use is associated with delinquent behavior, emotional problems such as anxiety or depression, and social skill deficits. Environmental influences are present in the contexts of the family, peer network, school, and neighborhood. For example, high levels of parental substance use, low parental supervision, and inconsistent family discipline are linked with elevated risk for using alcohol and illicit drugs. Association with deviant peers and peer substance use are consistently strong predictors of adolescent substance use. School-level influences include low academic achievement and low commitment to education. Neighborhoods characterized by high levels of poverty, crime, and drug availability are also associated with elevated rates of substance use among youth. The multidetermined nature of adolescent substance use suggests the need for comprehensive services that can address the various factors associated with this problem behavior.

LONG-TERM DELETERIOUS EFFECTS

Adolescent substance use is linked with a range of negative outcomes (Biglan, Brennan, Foster, & Holder, 2004). For example, adolescents who use alcohol and/or drugs are more likely than their non-substance-using peers to drop out of school early, which limits their opportunities to obtain employment later in life. Adolescents who use substances are also more likely to report earlier initiation of sexual activity, engagement in sexual activity with multiple partners, and inconsistent condom use, placing them at elevated risk for unplanned pregnancy and for contracting sexually transmitted diseases. Substance use also plays a role in other serious adolescent problem behaviors, such as motor vehicle accidents and suicide. Such findings highlight the need for effective interventions.

EVIDENCE-BASED INTERVENTIONS

Until the mid-1980s, relatively few interventions for adolescent substance abuse had received empirical support. After that time, however, several treatment approaches were developed and validated in randomized clinical trials. These include four family therapy models and cognitive behavioral therapy (CBT) delivered in individual and group formats.

Family Therapy. Although a wide and highly diverse range of family therapy models have been developed, four have emerged as having the most empirical support (Waldron & Turner, 2008): multisystemic therapy, functional family therapy, multidimensional family therapy, and brief strategic family therapy. These treatments share several important features. They each (a) are comprehensive and address known risk factors for substance use, (b) view the family as the primary vehicle for achieving favorable outcomes, (c) provide services in community-based settings, (d) use behavioral treatment principles, and (e) rely on strong quality assurance procedures to support therapist adherence to the treatment models.

Multisystemic Therapy. Multisystemic therapy (MST; Henggeler et al., 1998) is a comprehensive family- and community-based treatment for youth with serious substance use and delinquent behavior problems and who are at imminent risk of out-of-home placement. Treatment is provided by therapists using a home-based model of service delivery. Drawing upon evidence-based intervention strategies (e.g., CBT, pragmatic family therapy approaches), MST therapists individualize interventions to address the individual, family, peer, school, and neighborhood factors that are linked with the youth's behavioral and substance use problems, with caregivers viewed as the keys to achieving positive outcomes. For example, parent training techniques are often used to improve caregivers' ability to monitor their youth's whereabouts and provide consistent discipline. Similarly, with guidance from the therapist, caregivers also develop strategies to improve their youth's school performance, decrease his or her involvement with delinquent peers, and increase his or her participation in positive social activities (e.g., sports, church youth groups). Contingency management (CM), a widely supported

substance abuse intervention with adults (Higgins, Silverman, & Heil, 2007), has been effectively integrated with MST to accelerate abstinence (Henggeler et al., 2006). Sheidow and Henggeler (2008) provide a detailed summary of MST substance-related outcomes with serious juvenile offenders and substance abusing juvenile offenders.

Functional Family Therapy. Functional Family Therapy (FFT; Alexander et al., 1998) includes three phases of intervention: (1) engagement and motivation, (2) behavior change, and (3) generalization. During the engagement and motivation phase, therapists work to create a positive therapist-family relationship and to increase motivation for change by behaving respectfully toward family members and working to reduce anger and other negative emotions among family members. During the behavior change phase, therapists use parent training, family communication training, problem-solving skills training, and behavioral contracting to improve family relations in ways that lead to positive changes in youths' behavior, including substance use. During the generalization phase, therapists work to maintain clinical improvements by linking families with longer-term support services in the community (e.g., mental health, social service agencies).

Multidimensional Family Therapy. Multidimensional Family Therapy (MDFT; Liddle, Dakof, & Diamond, 1991) is a multi-component intervention that aims to reduce adolescent substance use by intervening directly with the adolescent and with the multiple systems that influence his or her behavior (e.g., family, peer network, school). During the initial stages of treatment, therapists try to develop a strong working relationship with the family and conduct a comprehensive assessment of the adolescent's substance use and other problem behaviors. Therapists subsequently work to bring about positive changes through the use of individual- and systems-level interventions. For example, individual therapy is conducted with the adolescents to improve their emotional and behavioral functioning and drug refusal skills. In addition, individual sessions are conducted with caregivers to improve their own emotional well-being, access to social support, and family management practices. Family sessions focus on improving the caregiver-adolescent relationship, and community-level advocacy is conducted to enhance family members' interactions with external sources of influence (e.g., school staff, peers, juvenile justice system personnel).

Brief Strategic Family Therapy. The underlying principle of brief strategic family therapy (BSFT; Szapocznik & Kurtines, 1989) is that adolescent substance use results from maladaptive interactions within the family. BSFT includes three primary intervention components: joining, diagnosis, and restructuring. In the early phases of treatment, the BSFT therapist works to join with the family by establishing a close therapeutic relationship with each participating family member. Over time, the therapist develops hypotheses about the family's diagnosis, which refers to those interactional patterns that encourage adolescent problem behavior. For example, the therapist might determine that adolescent substance use is influenced, in part, by inconsistent discipline and poor communication between the adolescent and his or her caregivers. Once identified, the BSFT therapist works to restructure these maladaptive family interactions using various techniques such as reframing, boundary setting, and communication skills training.

Individual- and Group-Based Cognitive Behavioral Therapy. Individual- and group-based CBT interventions are based on principles of social learning theory. According to this theory, adolescents may begin using alcohol or illicit drugs because this behavior is modeled by others in their home, school, or community. Once initiated, substance use can be maintained by a variety of factors. For instance, adolescents might continue to use substances because they produce pleasant feelings, help relieve anxiety or stress, or help the youth gain acceptance from peers.

Whether delivered in an individual or group setting, CBT interventions are designed to teach adolescents how to identify internal (e.g., stress) and environmental (e.g., parties) triggers for substance use and to develop strategies for avoiding those triggers. Adolescents are also taught various drug refusal and problem-solving skills as well as more positive strategies for coping with stress and anxiety. In some CBT interventions, motivational techniques are used during the initial sessions to help motivate adolescents to change their behavior. Unfortunately, and in

contrast with the aforementioned family therapy models, many of the family, peer, and community-level risk factors for adolescent substance use are rarely addressed directly in the context of CBT. Nevertheless, several individual- and group-based CBT interventions have received empirical support (Waldron & Turner, 2008).

It should be noted, however, that there is debate in the field regarding the use of group treatment for adolescents with substance use and other externalizing behavior problems. A few early studies found that the aggregation of antisocial adolescents in groups can actually intensify their problem behavior (Dishion, McCord, & Poulin, 1999). Other investigators, however, have reported positive effects of group treatment for substance-abusing adolescents (Burleson, Kaminer, & Dennis, 2006; Waldron et al., 2001). Some theorists have hypothesized that the likelihood of negative effects of group treatment probably depends on the level of structure of the group and the skill level of the group leader (Dishion & Dodge, 2005). Nonetheless, more research is needed to help reconcile these discrepant findings.

FREQUENTLY USED TREATMENTS WITH LITTLE EMPIRICAL SUPPORT

Despite the frequent use of residential, inpatient, and twelve-step (i.e., Alcoholics or Narcotics Anonymous) programs in the adolescent substance-use treatment field, their effectiveness has not been established in rigorous research (Brown & Abrantes, 2006). Residential and inpatient interventions might be indicated if the adolescent poses significant safety concerns and his or her needs cannot be addressed in a less restrictive environment. Reviewers have noted, however, that the long-term effects of these restrictive interventions may be limited (American Academy of Child and Adolescent Psychiatry, 2005). For example, in light of the multiple family- and community-level risk factors for adolescent substance use, removing youth from their natural environment (sending them to residential treatment) without altering that environment will likely result in only temporary reductions in substance use. Once youth are discharged from these programs, they often resume their substance use because the factors that support such use (i.e., family, peer, school, and neighborhood influences) have not been addressed. Finally, some data suggest that twelve-step programs can be helpful when used as an adjunct to more formal treatment (Williams & Chang, 2000), although these programs have not been evaluated in controlled studies.

Extensive research has documented the prevalence and correlates of alcohol and drug use among youth, and this body of work strongly supports the view that substance use is multi-determined, involving influences at multiple environmental levels. Based largely on this research, several family-based treatments were developed, and these proved effective in reducing adolescent substance use. Individual- and group-based CBT interventions also emerged as having some empirical support. Although widely used, scant evidence supports the effectiveness of residential, inpatient, and twelve-step programs, and additional research was needed as of 2008 to determine the short- and long-term effects of these approaches.

See also **Adolescents and Drug Use.**

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OLDER ADULTS

In the United States and many other nations, older adult populations are growing rapidly. "Older adults" have been variously defined in the literature, ranging from age 50 and over to age 65 and over. According to the U.S. Census Bureau (2003), by the year 2030, approximately 69 million Americans will be age 65 or older. Along with a growing demand for other health-care services, the substance abuse treatment needs of older adults are also increasing. For example, a 2003 study analyzed the growth in the size of the older population, taking into consideration the levels of alcohol and drug consumption among baby boomers (which are higher than those of the current elderly cohort), and projected that the number of adults age 50 and over in need of drug and alcohol abuse treatment will double by 2023 (Gfroerer et al., 2003).

RISKS FOR OLDER ADULTS

Researchers and clinicians are becoming more aware of the specific alcohol and drug problems experienced by older adults, and they have begun to develop strategies to address the specific treatment needs of this population, particularly in regard to the substantial medical, social, and personal costs associated with alcohol and drug problems in older adults, which include gastrointestinal, cardiovascular, endocrine, and neurological disorders (Gambert & Katsoyannis, 1995). Because alcohol sensitivity increases with age, older adults are more vulnerable than younger adults are to these problems. Further, the risks of delirium, adverse medication interactions, and falls are also increased in this age group. Finally, as is true for the population in general, a substantial number of older adults who commit suicide have a history of alcohol dependence (Waern, 2003).

Alcohol remains the most common substance of abuse among older adults. In community samples, the prevalence of alcohol abuse or dependence is approximately 1 percent to 3 percent for men over age 65, and .5 percent to 1 percent for women over

65 (Bucholz, Sheline, & Helzer, 1995). Due to the medical and psychiatric disorders associated with heavy alcohol use, clinical samples have consistently shown an even higher prevalence. Prescription drug misuse by older adults is also a significant concern, because older adults are more likely than younger adults to take several medications concurrently. Older adults are among the patient groups at highest risk for the misuse of medications resulting in dependence (Simoni-Wastila & Strickler, 2004). When using multiple medications, adverse drug interactions (or interactions between drugs and alcohol) are also potential problems, due to the greater number of medications taken by this population, as well as their greater vulnerability to adverse drug reactions.

SCREENING AND TREATMENT REFERRAL

The identification of alcohol or drug abuse can be more challenging in older adults than it is in younger populations. Older adults tend to drink at home and are less likely than younger adults to draw the attention of law enforcement, the courts, and the other agencies that often refer younger people to alcohol and drug treatment services. Older people are also less likely to have noticeable problems at work, school, or childrearing, mainly because they are less likely to have these types of responsibilities. As a result, there is a reduced visibility of addiction among older adults, and thus fewer opportunities to identify older patients in need of treatment.

Medical and social service appointments are important screening opportunities. A study of adults in a managed care outpatient program found that older patients were more likely than younger patients to report that a physician encouraged them to enter the program (Satre, Mertens, Areán & Weisner, 2003). In contrast, younger adults were more likely to report that an employer had recommended treatment. This suggests that health providers play an especially important role in helping to motivate older adults to seek treatment.

The Center for Substance Abuse Treatment has recommended that all older adults be screened for alcohol misuse during routine medical appointments. This provides an opportunity to identify those in need of specialized services. When screening, providers should ask older adults how much they typically drink, keeping in mind that no more than one standard drink per day is recommended for men and women over age 65. In addition to questions regarding quantity and frequency of alcohol consumption, screening instruments may be helpful in determining the severity of any problems (Fink et al., 2002). Where significant misuse of alcohol or a dependence on prescription or illegal drugs is present, referral to an outpatient or residential treatment program may be appropriate.

STUDIES OF OLDER ADULTS IN TREATMENT

There is, however, comparatively little research on treatment outcomes among older populations. Studies conducted in mixed-age settings have found that older adults stay in treatment longer and have post-treatment abstinence outcomes as good as or better than those of younger adults. In a study conducted in a large managed care outpatient program that included 12-step and relapse-prevention components, older patients had several clinical characteristics associated with good outcomes (Satre, Mertens, Areán & Weisner, 2003). Older adults (age 55 and over) had lower rates of drug dependence (versus dependence only on alcohol), scored lower on a hostility measure, and were more likely to state that total abstinence (versus controlled use) was their goal of treatment, compared with adults aged 18 to 39. These factors were associated with abstinence six months post-treatment. Thus, the study helped to demonstrate some of the strengths that older adults may bring to treatment.

Even though older adults appear to succeed reasonably well in mixed-age settings, limited research suggests that they may do even better in treatment settings where only older adults are present (Blow, 1998; Kofoed et al., 1987). For one thing, age-specific groups may facilitate sharing between patients with similar life experiences and treatment issues. However, funding constraints may limit many service agencies from providing a wholly separate treatment program for older adults. Within mixed-age chemical dependency programs, therefore, it may be beneficial (and more feasible) to provide a weekly group session for older patients as a supplement to other clinic services.

The lack of women in studies of treatment for older adults creates a significant gap in the

literature (Blow, 2000). Because much of the treatment outcome research has been conducted in Veteran's Administration programs, women have generally not been included. However, some studies have examined gender differences among older adults in treatment. One study looked at gender differences among alcohol-dependent adults aged 55 and over in outpatient treatment at Kaiser Permanente (Satre, Mertens & Weisner, 2004). Both clinical characteristics and abstinence outcomes were examined in this study. At the point of treatment entry, women and men had comparable drinking levels, although the women reported a later onset of heavy drinking. Women, however, stayed in treatment longer and had significantly higher rates of abstinence six months following treatment than men. While further research is needed, these findings show that clinically important gender differences may exist among older adults in treatment.

TREATMENT STRATEGIES

Service providers addressing alcohol and drug problems in older adults should take into account the specific needs of the individual, such as severity of addiction and overall level of functioning. Not all patients may need formal substance abuse treatment. Older adults considered "at risk" of developing alcohol-related health problems because they drink above recommended limits but do not meet criteria for substance abuse or dependence appear to benefit from brief interventions to reduce drinking (Fleming et al., 1999). Such individuals are not likely to seek out formal treatment, but they may come to the attention of health and social service agencies, especially if providers conduct regular screening. For these older adults, brief interventions (usually one to five sessions) are designed to motivate individuals to limit the amount of alcohol they consume. The interventions focus on health effects and other problems associated with alcohol misuse, and they are effective in reducing drinking to safer levels (Blow and Barry, 2000). These sessions may be conducted in primary care or other settings where adults receive services.

In traditional outpatient alcohol and drug treatment settings, relatively straightforward adaptations that consider patient age can substantially increase treatment effectiveness. For example, to accommodate possible hearing loss and cognitive changes (if these are present), it may be helpful to speak slowly and more loudly, use simpler language, and present information at a slower pace, with frequent repetition of material to assist in learning (Satre, Knight & David, 2006). Assistive listening devices such as earphones and an amplifier may be useful with hearing-impaired patients. In a group context, it may be necessary for leaders to be more active and provide more structure than they would with younger patients. This could include taking the lead in introducing topics for discussion or encouraging relatively quiet group members to participate more fully.

Confrontational tactics do not generally work well with older patients. A better approach is to increase motivation by focusing on the reasons for older people to maintain sobriety. These include maintaining independence and good health, improving financial security, avoiding depression, and repairing relationships with family members who may have become estranged in the course of addiction. These concerns are generally applicable in treatment.

Topics that should be addressed in the treatment of older adults may be somewhat different than those that are important in working with younger patients. For example, the loss of a spouse or partner may lead to increased drinking among individuals who may already have been heavy consumers of alcohol. Such patients are likely to be struggling with grief, and they may therefore need to use some of their session time to explore their feelings of loss. In addition, an important treatment task for these patients is to identify new sources of social support. A development of more effective coping strategies will help to reduce their reliance on alcohol or drugs in coping with feelings of sadness. Retirement is another potentially stressful late-life transition, and some retirees may cope with the end of a career by increasing their drinking. Other issues to address in treatment may include housing problems, decreased physical mobility, and comorbid depression and anxiety. To help address these challenges, the coordination of substance abuse treatment with medical and social services is highly desirable.

CONCLUSION

Drug and alcohol abuse pose a significant threat to the health and well-being of older adults, and prevalence is likely to increase with the aging of the baby boom generation. For these reasons, health and social service providers should be attentive to the potential for substance misuse among older adults. Fortunately, there is evidence that older adults benefit from interventions to reduce harmful drinking or drug use. Studies in this area strongly support screening for substance problems among older adults, particularly in medical and social service contexts. For those with an alcohol or drug problem, brief interventions or referral to formal substance abuse treatment programs may be effective.

Clinicians working in the alcohol and drug abuse treatment field have a responsibility to understand the specific treatment needs of older patients. Adaptations of existing treatment strategies to suit the special needs of older patients are likely to be useful in providing services to this important and rapidly growing population.

See also **Aging, Drugs, and Alcohol; Alcohol; Complications: Cognition; Prescription Drug Abuse; Risk Factors for Substance Use, Abuse, and Dependence: An Overview; Treatment: An Overview of Alcohol Abuse/Dependence; Treatment: An Overview of Drug Abuse/Dependence; Treatment, Stages/Phases of: Screening and Brief Intervention.**

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THERAPEUTIC COMMUNITIES

Therapeutic communities (TCs) are drug-free residential treatment facilities for drug and/or alcohol addiction. TCs emerged in the 1960s as a self-help

alternative to the conventional medical and psychiatric approaches being used at that time.

Most traditional TCs have similar features, including their organizational structure, staffing patterns, perspectives, rehabilitative regimes, and a twelve- to eighteen-month duration of stay. They differ greatly, however, in size (30–600 beds) and client demography. Most people entering TCs have used multiple drugs—including tobacco, marijuana, alcohol, opiods, pills, and, recently, cocaine and crack-cocaine. In addition to their substance abuse, most TC clients also have a considerable degree of psychosocial dysfunction (Jainchill, 1994). In traditional TCs, 70 to 75 percent of clients are men, but admission for women is increasing. Most community-based TCs are integrated across gender, race/ethnicity, and age. Primary clinical staff are usually former substance abusers who were rehabilitated and trained. Other staff are the professionals who provide medical, mental health, vocational, educational, family-counseling, fiscal, administrative, and legal services.

Traditional TCs share a defining view of substance abuse as a deviant behavior, which may be attributed to psychological factors, poor family effectiveness, and, frequently, to socioeconomic disadvantage. Drug abuse is thus seen as a disorder of the whole person and recovery as a change in lifestyle and personal identity. As part of the recovery process, TCs seek to eliminate antisocial attitudes and activity, develop employable skills, and inculcate prosocial attitudes and values. This TC view of recovery is based upon several broad assumptions: the client's motivation to change, the client's main contribution to the change process (*self-help*), the mediation of this recovery through peer confrontation and sharing in groups (*mutual self-help*), the affirmation of socially responsible roles through a positive social network, and the understanding that treatment is a necessarily intense "episode" in a drug user's life.

Diverse elements and activities within the TC foster rehabilitative change. Junior, intermediate, and senior peer levels stratify the *community*, or the family. The TC's basic program elements, consisting of individual counseling and various group processes, make up the therapeutic and educative elements of the change process. The daily activities, including morning meetings, seminars, house meetings, and general meetings facilitate assimilation into the community as a *context for social learning*. Clients are oriented into the program during the *orientation-induction* stage. They progress through the *primary treatment* stage of the program by achieving plateaus of stable behavioral change. Client development reflects their changing relationship with the community, characterized as *compliance, conformity*, and *commitment*. Finally, *reentry* represents the final program stage where the skills needed in the greater social environment are fostered through increased self-management and decision making.

The effectiveness of the traditional long-term residential TC, as described here, has been well-documented (De Leon, 1997, 2000). Today, TCs include a wide range of programs serving diverse clients who use a variety of drugs and present complex social/psychological problems. Client differences, clinical requirements, and funding realities have all encouraged the development of modified residential TCs with shorter stays (3, 6 and 12 months) as well as TC-oriented day treatment and outpatient models. Most traditional TCs have expanded their social services or incorporated new interventions to address the needs of special populations such as adolescents, mothers and children, homeless, mentally ill chemical abusers, and prison inmates. In these modifications the cross-fertilization of personnel and methods from the traditional TC, mental health, and human services portends the evolution of a new therapeutic community.

See also **Sobriety.**

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GEORGE DE LEON

TREATMENT, STAGES/ PHASES OF

This entry includes the following essays:

INITIATION OF ABSTINENCE

Individuals recovering from substance-use disorders (SUD), irrespective of treatment type (e.g., 12-step or cognitive behavioral) or modality (e.g., outpatient, inpatient, detoxification, or residential), achieve significant improvement in their substance-use behavior, including becoming abstinent, via various pathways. For example, it is not uncommon for individuals to significantly reduce their substance use prior to initiating treatment, as reported by Elizabeth E. Epstein and coworkers (2005), and Jon Morgenstern and colleagues (2007). Alternatively, some individuals do not significantly improve their substance-use behavior until after extensive treatment and/or participation in self-help groups (e.g., Alcoholics Anonymous or Narcotics Anonymous). In addition, many people substantially improve their substance-use behavior in response to undergoing assessment for their substance use, which contributes to both clinical improvements (e.g., reduced substance use; Clifford et al., 2007) and enhanced treatment participation (Maisto et al., 2007a).

Although it is likely that significant differences exist between early and late treatment responders, as well as differences between those substance users who modify their behavior with and without professional assistance, relatively little is known about the factors that differentiate these groups. Likely factors in this distinction include biological susceptibility; environmental factors such as unemployment, homelessness, and social support; clinical factors such as comorbidity and SUD severity; and personal factors such as the motivation to change and self-efficacy.

Individuals receiving treatment for SUD often achieve significant but varying periods of abstinence interspersed with periods of problematic substance use and psychological and/or social distress. It is not clear to what extent changes in substance use are associated with changes in other areas of functioning (e.g., employment) or how these distinct domains of functioning are related temporally. A major challenge facing clinicians who treat substance users is the maintenance of behavioral change, particularly a reduction in substance use. In this regard, it appears that the first year following treatment initiation is a critical period. For example, Stephen A. Maisto and colleagues (2007b) investigated the stability of alcohol-use patterns across Project Match's three-year follow-up period and found that 71 percent of subjects who abstained during the first year reported still being abstinent at three years, 69 percent of the heavy drinkers continued to drink heavily, and 50 percent of the moderate drinkers reported either continued moderate alcohol use or abstinence.

James R. McKay and Richard V. Weiss (2001) reported that SUD treatment outcomes were associated with client treatment performance and pro-recovery behaviors (e.g., coping or self-help participation). As with alcohol treatment outcomes, the first year following drug treatment may be especially important with respect to longer-term substance use. D. Dwayne Simpson and colleagues (2002), for example, reported that among a national cocaine treatment sample, the large decreases in cocaine use observed one year post-treatment were sustained at the year five follow-up.

Thus, it appears that no specific treatment stage or phase may be associated with the onset of abstinence; rather, abstinence can, and does, occur at any point. What appears to be important for better longer-term functioning is a period of sustained abstinence, or at least the avoidance of frequent heavy substance use, particularly during the initial one-year post-treatment period.

See also **Alcoholism: Abstinence versus Controlled Drinking.**

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MEDICAL DETOXIFICATION

Medical detoxification can be defined as the use of medical interventions to facilitate safe withdrawal from psychoactive substances. Implicit in the term is the assumption that alcohol and drugs are toxic and the process of recovery must involve the removal of these toxins and their effects from the system. Besides its role in individuals addicted to a substance, detoxification may also be necessary in some patients who may not be addicted in the behavioral sense but have developed physiological dependence due to extended treatment with certain medications, such as opioid pain medications or sedative-hypnotic medications for anxiety or insomnia.

NEUROBIOLOGICAL BASIS

When a person consumes a psychoactive substance, it induces changes in brain neurotransmitter systems. After repeated use of the substance, adaptive mechanisms come into play in an effort to restore the balance. This can manifest clinically as tolerance (the need to use increasing amounts of the substance to achieve the same effect). A related, but different, phenomenon is seen when the individual tries to stop using the substance. In this case the adaptive mechanisms operate unchecked, causing a withdrawal syndrome, which generally involves symptoms that are opposite those of the major effects of the substance. These symptoms emerge and peak over a period of several hours to days, depending on the half-life of the substance, and then gradually diminish as balance is reestablished. All symptoms may not resolve at the same rate, and some individuals may have a prolonged period of discomfort, sometimes referred to as protracted withdrawal.

PROCESS OF MEDICAL DETOXIFICATION

The primary goal of detoxification is to safely and effectively manage the withdrawal symptoms that can emerge upon cessation or reduction of the use of a psychoactive substance. Individuals with lesser degrees of physiological dependence may stop using a substance on their own with no adverse effects. In a treatment setting, detoxification should be preceded by a careful evaluation of the patient, including the substance(s) used; the duration, quantity, and frequency of use; the time of last use; and any medical and psychiatric risk factors.

The process of medical detoxification varies depending on the substance and involves three major components: monitoring, supportive measures, and medication. It may take place in outpatient or inpatient settings, based on the substance(s) involved, the anticipated severity of withdrawal, the availability of support and monitoring in the patient's home environment, the patient's general physical condition, and the presence of associated medical and psychiatric disorders. Rating scales to assess severity of withdrawal from specific substances, such as the Clinical

Institute Withdrawal Assessment for Alcohol Scale-Revised (CIWA-Ar; Sullivan et al., 1989) and the Clinical Opiate Withdrawal Scale (COWS; Wesson & Ling, 2003), may be used to guide the detoxification process.

DETOXIFICATION FROM SPECIFIC SUBSTANCES

Alcohol. Withdrawal from alcohol and sedative-hypnotics (substances that depress the functioning of the central nervous system) can be serious, and even life-threatening in a small proportion of patients. The symptoms and signs of withdrawal may range from more minor—including tremor ("shakes"), anxiety, and elevated pulse and blood pressure—to more severe—such as auditory, visual, or tactile hallucinations; seizures; and delirium tremens (a combination of delirium and confusion, agitation, disorientation, and tremor). Delirium tremens is a serious condition with an associated mortality of approximately 1 percent (Mayo-Smith et al., 2004). Patients at the highest risk of severe withdrawal are those with a history of prolonged heavy drinking, those in poor physical condition with associated medical problems, and those with a history of prior severe withdrawal episodes. The symptoms usually emerge within a few hours (but may not emerge until three to four days after the last drink), peak over the next two to three days, and then resolve over four or five days.

Patients at risk of severe withdrawal may require management in an inpatient unit under medical supervision. Supportive measures such as the monitoring of vital signs and level of consciousness, the maintenance of fluid and electrolyte balance, and precautions against falls, together with other protective measures, may be needed. Medication management typically includes benzodiazepines such as diazepam (Valium), chlordiazepoxide (Librium), or lorazepam (Ativan). These are tapered off as the patient's condition improves. Many patients who drink heavily are nutritionally deficient, and some may develop complications such as Wernicke's encephalopathy, a condition caused by a thiamine (Vitamin B1) deficiency. If untreated, it may result in Korsakoff syndrome, which is a highly disabling, often irreversible, disorder of memory. Giving thiamine supplements routinely to all patients with a history of heavy alcohol consumption can effectively prevent this complication.

Sedatives and Hypnotics. The features of sedative-hypnotic withdrawal are similar to those of alcohol withdrawal, but with some noteworthy differences: Onset may be within hours of the last use of a short-acting drug such as alprazolam (Xanax), or delayed for several days for long-acting drugs such as diazepam or phenobarbital. There is also a greater risk of withdrawal seizures, particularly from the shorter-acting substances; the withdrawal symptoms often intensify during the later part of the detoxification process; and the process may need to be extended over weeks, or even months in some patients. Two main approaches are utilized for detoxification: (1) tapering down the dose of the substance being abused, or (2) switching to an equivalent dose of a long-acting benzodiazepine or barbiturate (such as diazepam or phenobarbital, respectively), which is then slowly tapered off (Center for Substance Abuse Treatment, 2006, pp. 75–78). Because of the risk involved in sedative-hypnotic detoxification, it is generally better done under the supervision of a specialist, particularly when the patient has been abusing large amounts of the substance over a long period.

Opioids. Withdrawal from opioids (such as heroin, methadone, and narcotic pain medications) can be painful and distressing, but is rarely life-threatening except in debilitated individuals. It somewhat resembles a severe case of influenza, with body ache, back pain, watering of the eyes, runny nose, sneezing, yawning, diarrhea, abdominal cramps, nausea, vomiting, elevated blood pressure and pulse, dilated pupils, gooseflesh (hence the term *cold turkey*), and jerky movements of the legs (giving rise to the expression *kicking the habit*). The time of onset with a short-acting opioid such as heroin is six to eight hours after the last use, with a peak on the second or third day; withdrawal symptoms diminish by the fourth or fifth day. Withdrawal from a longer-acting opioid such as methadone may be delayed for up to two or three days and may last two or three weeks.

Several approaches are used to minimize the symptoms and shorten the duration of withdrawal. Most commonly, a full or partial opioid agonist medication (such as methadone or buprenorphine, respectively) is started and slowly tapered off over five to seven days. Another approach utilizes clonidine, which helps to reduce anxiety, blood pressure, and

pulse rate, along with adjunctive medications for other withdrawal symptoms. Sometimes, an opioid antagonist (such as naltrexone) is utilized with clonidine to shorten the detoxification process (this is known as rapid opioid detoxification). A more aggressive, and potentially more risky, approach involves administering an opioid antagonist to precipitate acute withdrawal after placing the patient under general anesthesia; its practitioners claim that it shortens the withdrawal duration to just a few hours (called ultra-rapid opioid detoxification). Whatever the approach used for detoxification, there is a high risk of relapse without extended aftercare engagement. There is also a greater risk of accidental overdose, and possible mortality, after voluntary or involuntary detoxification (such as during a hospitalization or incarceration) as the patient's tolerance to opioids is diminished. For these reasons, long-term maintenance on methadone or buprenorphine may be preferred for patients willing to engage in it.

Stimulants. Cocaine and amphetamine withdrawal consists of prominent symptoms such as mood, sleep, and appetite disturbances; psychomotor agitation or retardation; fatigue; and intense cravings. Detoxification primarily involves supportive measures. Suicidal behavior can occur during this period and may last several days, occasionally necessitating a brief inpatient stay.

Other Drugs. The American Psychiatric Association's *Diagnostic and Statistical Manual, Text Revision* (2000) does not recognize clinically significant withdrawal syndromes for cannabis, hallucinogens, phencyclidine, or inhalants. However, there is growing evidence that a cannabis withdrawal does occur, with anxiety, restlessness, irritability, anger, strange dreams, decreased appetite, and weight loss as its main symptoms. Most symptoms begin within 24 hours of abstinence, peak within the first week, and last approximately one to two weeks. Little research has been done on the management of these symptoms.

It is a common misconception that detoxification constitutes a stand-alone treatment for drug addiction. Although it is often a necessary first step in the recovery process, detoxification by itself is nearly always insufficient to achieve long-term abstinence and recovery from addiction. Medical detoxification reduces the discomfort experienced by the patient and the risk of more serious adverse consequences. It also provides an opportunity to establish a therapeutic alliance and engage the patient in long-term, recovery-oriented treatment.

See also **Addiction: Concepts and Definitions; Treatment: An Overview; Treatment, Pharmacological Approaches to: Clonidine; Treatment, Stages/Phases of: Non-Medical Detoxification; Withdrawal: Alcohol.**

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NON-MEDICAL DETOXIFICATION

The term *detoxification* can refer to the management of two distinct types of problems resulting from excessive alcohol or other drug use. These are the physical and behavioral symptoms of intoxication on the one hand or of withdrawal following a prolonged period of substance use on the other. Although both involve recovering from the toxic effects of a drug while refraining from further use, the problems associated are dissimilar and require different management approaches. Non-medical approaches have been developed for the management of both intoxication and withdrawal that for

most people are equally as safe and effective as more expensive medical approaches.

In most countries alcohol and other drug problems are so widespread that cost containment in healthcare becomes a priority. This requirement rules out an exclusive reliance on expensive medical settings, medical personnel, and medication. A number of relatively safe and cost-effective alternatives to inpatient hospital care have been devised that are frequently preferred by clients and also have other advantages. Despite research evidence for equivalent effectiveness and some tangible advantages, non-medical detoxification remains unavailable in some healthcare systems because only hospital-based medical detoxification is eligible for payment from state or private health funds.

MANAGING PUBLIC DRUNKENNESS

The most visible problems associated with extreme intoxication concern public order, particularly in relation to the use of alcohol. Drunkenness is associated with violence both to the self and to others as well as with public nuisance offenses. The habitual drunken offender and the potentially dangerous disorderly drunk present themselves in large numbers to police forces the world over, placing a substantial burden on criminal justice systems. For this reason a number of countries have experimented with decriminalizing public drunkenness. There is also a growing awareness that locking intoxicated people in police cells puts them at risk of serious harm. In Australia, for example, the tragic deaths of many Aboriginal people while in police custody are thought to have been caused by the combined effects of alcohol and confinement.

Setting up non-medical detoxification services has sometimes occurred hand-in-hand with decriminalization of drunkenness. Early pioneers in the 1970s were the Addiction Research Foundation in the Canadian province of Ontario and St. Vincent's Hospital in New South Wales, Australia. In both cases services were set up with the principal aim of diverting drunkenness offenders from the criminal justice system to a more humane setting where they might receive counseling and support. Both utilized a residential social setting staffed by non-medical personnel and provided no medical care or medication. When fully functioning, these services successfully supervised thousands of problem drinkers, mainly self-referred, through sobering-up and/or alcohol withdrawal with an impressive record of safety. In its first ten years of operation, the New South Wales facility dealt with nearly 14,000 admissions and recorded only two fatalities among this high risk population (Pedersen, 1986). Only 1 percent of admissions required transfer to a nearby hospital for specialized medical care, often for reasons unrelated to alcohol withdrawal. Sandra C. Lapham et al. (1996) describe a model of drug-free management of alcohol withdrawal in a sample of 160 homeless men and women with alcohol withdrawal signs who were admitted to a non-medical residential setting in New Mexico. Most experienced minor symptoms and only two required referral to a medical facility. The rest were managed safely without medication and without serious complications.

SOBERING-UP AND WET SHELTERS

In designing detoxification services, intoxication and withdrawal should not be confused. While highly successful and cost-effective alternatives to hospital care for alcohol withdrawal exist, they are not the panacea for problems posed by habitual drunken offenders. Australia's continuing concern to prevent Aboriginal deaths in custody has also prompted an increasing use of what have come to be called *sobering-up shelters*. These are supportive non-medical settings where people can stay a few hours or, if necessary, overnight until they are sober. They provide an inexpensive alternative to prison and have gained the necessary support of the local police (Drug and Alcohol Office, 2007). Sobering-up shelters need access to specialist treatment facilities, so they can refer people requiring urgent medical attention or longer-term help with a drinking problem.

There are potentially serious medical emergencies associated with extreme levels of drug intoxication. Poisoning through overdose, accidental or otherwise, is a common cause of admission to hospital emergency rooms the world over and all too frequently this results in death. Overdosing on heroin can also be quite common where that drug is widely used, especially if users have lost tolerance to the drug's effects after a period of abstinence, if it is used with other CNS depressant drugs such as alcohol or benzodiazepines, and/or if the heroin is unusually pure. For this reason staff of sobering-up

shelters, or of any facility that also caters to drug users, should be trained to identify warning signs of overdose so that the sufferer may be taken to a hospital with as little delay as possible. In some countries the opiate-antagonist drug naloxone is used in a variety of non-medical settings, including by drug-using peers at the scene of an overdose (Baca and Grant, 2005). Similarly, there is a great educational need among the general drug-using and drinking public who may abandon their friends to "sleep it off" only later to find them asphyxiated.

A relatively recent approach to the management of homeless, habitual drunken offenders in Canada and the United Kingdom is the establishment of *wet shelters*, where alcohol is provided freely in regular, measured doses throughout the day for residents with established levels of alcohol dependence. This stabilizes clients and reduces the risk both of intoxication and withdrawal with all their attendant complications (Podymow, 2006). Similar programs have been developed in the state of Washington that allow residents to continue their drinking and have alcohol on the premises, although it is not directly provided to them. This *harm reduction* approach to the management of serious alcohol-related problems mirrors that used in *safe consumption* or *safe injection* sites for injecting drug users in a number of European cities as well as Canada. These can reduce the risk of fatal drug overdoses as well as the transmission of blood-borne viruses (Health Canada, 2008).

MANAGING ALCOHOL AND OTHER DRUG WITHDRAWAL

Detoxification services exist on a continuum ranging from supervision by an informed lay person (a relative, a recovered problem drinker or user, or non-medical professionals) all the way to 24-hour nursing and medical care in a specialist hospital unit. Even in the latter case, substantial variations exist regarding the amount of medication used during withdrawal, or even whether any medication is used at all. Detoxification services designed to minimize discomfort and the possibility of actual harm occurring during withdrawal may be non-medical in several senses, either by using non-medical settings (e.g., hostels, the client's home), non-medical personnel (e.g., relatives, ex-problem drinkers), or non-medical procedures (e.g., alternative medicine approaches). There is wide consensus that medical assistance needs to be available if required, but the responsibility for providing this need not be left only with medical personnel.

An influential early North American study showed that in the relative safety of an alcoholism treatment unit only five percent of admissions required any form of medical assistance. In addition to the residential, *social-setting* model of detoxification, *ambulatory* or outpatient detoxification procedures that relied on the drinker calling in daily to a clinic to collect his or her medication and receive a brief check-up were developed. Evaluations of these types of service conducted in several countries have demonstrated that their success rate in terms of both safety and effectiveness is at least the equal of inpatient care and is considerably less expensive.

A variation of this approach, *home detoxification*, is an approach developed initially in the United Kingdom with problem drinkers and is now widely used in many other countries. This usually involves a community alcohol worker (e.g., nurse, counselor, or psychologist) assisting a family practitioner to assess a drinker who wishes to stop drinking alcohol but who may experience severe withdrawal symptoms in the process. Providing that the home environment is deemed supportive and the client is sufficiently motivated to stop drinking, the detoxification then occurs in the patient's home with visits from the alcohol worker. The family doctor's telephone number is provided to the client and any close relative or partner in case of emergency. A particular effort is made to screen out drinkers with a history of withdrawal seizures, delirium tremens, or Korsakoff's Psychosis. To reduce the risk of overdose with some types of medication (notably chlormethiazole), either the alcohol worker or a relative holds the medication. In the United Kingdom many family doctors were already prescribing chlormethiazole to cover alcohol withdrawal but without accompanying supervision and often longer than the recommended maximum period. This was the single most common method of managing alcohol withdrawal among a group of individuals who were loathe to enter a psychiatric hospital or specialized treatment unit. Later studies showed that home detoxification is more acceptable to groups that are frequently underrepresented in traditional treatment settings such as the young, the elderly, and women. Home detoxification therefore offers a safe alternative to completely unsupervised withdrawal on the

one hand and a cost-effective alternative to inpatient hospital care on the other. The cost of home detoxification per client has been estimated to be approximately one-quarter that of inpatient hospital care. Formal evaluations of the U.K. service suggest that not only is there no loss in terms of either safety or efficacy but that the clients prefer to be treated at home and that many would refuse admission to a hospital.

A consistent finding regarding nonmedical or social approaches to detoxification across several countries has been that they are not only equally safe but have the advantage of being more likely to result in clients being successfully referred for further treatment, whether residential or nonresidential. One U.S.-based review comparing traditional and nonmedical approaches to detoxification (Beshai, 1990) strongly recommended that both types of service were necessary and that screening should be conducted so that more severely dependent cases and those with a history of delirium tremens or withdrawal seizures can be referred on to specialist medical service providers.

CONCLUSIONS

Cost-effective, nonmedical approaches have been developed to manage both problems of intoxication and alcohol or other drug withdrawal. It is very important to be clear about the different objectives and issues to be managed in relation to these two core elements involved in detoxification. Both intoxication and alcohol withdrawal are so common in Western society that, although they carry a small but significant risk of serious injury or death, it is too costly to provide specialist medical care in every instance. Safe and inexpensive alternatives have been developed in a number of countries that are to be recommended over a laissez-faire or punitive approach to these major social problems. Encouraging evidence suggests that community-based detoxification services attract problem drinkers who are usually underrepresented in treatment services, such as women, young people, and the elderly. Furthermore, social or nonmedical detoxification has been found to be consistently superior to traditional medical inpatient care in terms of facilitating referral to ongoing support and follow-up services. It is important, however, to screen out individuals with a history of severe complications from alcohol withdrawal such as delirium tremens or seizures, who will normally require specialized medical care to safely manage the withdrawal process. There is only limited published research concerning the efficacy of such approaches for the management of problems with drugs other than alcohol.

See also **Antagonist; Australia; Britain; Britain: Alcohol Use and Policy; Canada; Delirium Tremens (DTs); Funding and Service Delivery of Treatment; Harm Reduction; Naloxone; Overdose, Drug (OD); Prevention, Education and; Treatment: Outpatient Versus Inpatient Setting; Withdrawal: Alcohol.**

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SCREENING AND BRIEF INTERVENTION

Screening and Brief Intervention (SBI) is an integrated approach to early intervention for individuals with substance-abuse disorders, as well as those who are at risk of developing them. SBI is sometimes included in a more comprehensive approach that adds referral to treatment (called SBIRT). SBI is based on public health procedures, as described by Thomas Babor and colleagues in 2007, designed to reduce the burden of injury, disease, and disability associated with the misuse of psychoactive substances, particularly alcohol, illicit drugs, tobacco products, and prescription medications with high abuse potential. SBI begins with the introduction of systematic screening in medical facilities and other community settings where people engaged in substance misuse are likely to be encountered (e.g., emergency rooms, community health clinics, social service settings). Screening is a preliminary procedure to evaluate the likelihood that an individual has a substance-abuse disorder or is at risk of negative consequences from the use of alcohol, tobacco, or other drugs. It may be conducted by means of interviews, questionnaires, or biological tests based on samples of blood, urine, hair, or saliva. Screening can also be conducted on a routine basis for all patients, or opportunistically with those who offer evidence of substance use because of their presenting symptoms or problems (e.g., high blood pressure or an injury resulting from a fight or motor vehicle accident).

Typically, SBI programs provide a brief intervention to individuals considered to be at elevated risk, and referral to further evaluation and treatment for those identified at high risk. The term *brief intervention* refers to any time-limited effort to change health behavior or attitudes in relation to substance misuse. When conducted in a medical setting, it usually consists of one to two visits or consultations lasting from 5 to 20 minutes. It generally takes the form of a short conversation between a substance user and a concerned physician, nurse, physician assistant, or social worker. The aim is to provide objective feedback about the results of the screening test, to give information about the health risks associated with continued substance use, to establish a goal for the patient to either stop or cut down use (depending on the substance), and to motivate the patient to work toward that goal through encouragement and support. Screening often identifies those who already have a substance-related health condition or a suspected substance-abuse disorder that warrants a formal diagnosis and possible referral to treatment. In these cases the brief intervention may take the form of referral advice and encouragement to seek treatment.

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RELAPSE PREVENTION

After an individual successfully decreases or abstains from a problematic behavior (e.g., drinking excessively, drug use, binge eating, pathological gambling), the risk of returning to a pre-change level of behavior remains. Relapse prevention (RP) is therefore an important component in maintaining the positive behavior change. The primary goals of RP are to: (1) provide the skills needed to anticipate risks and prevent an initial lapse, and (2) keep a lapse from becoming a full relapse. RP is based on research showing that there is an increased risk of

relapse following behavior change. Theories of relapse initially assumed a linear "if . . . then" relationship between risks and relapse, but more recent research has supported a dynamic model of relapse. This model includes the consideration that many factors interact with one another during high-risk situations. For example, cognitive processes (e.g., self-efficacy, expectations, motivation, and craving) interact with coping behaviors (e.g., cognitive-behavioral, approach-avoidance, self-regulation), affective states, and maladaptive behaviors. Identifying these interactions allows for more specificity in tailoring self-management skills to the needs of the individual.

There are many important components in RP, including recognizing high-risk situations, self-efficacy, motivation, coping skills, and social support. Assessing high-risk situations, including cues, triggers, and cravings, allows the development of individual-oriented plans to help avoid particular situations or implement other coping strategies. High-risk situations can include both external events (e.g., parties or celebrations) and internal states (e.g., anxiety or depression). Along with identifying these risky situations, identifying positive coping skills is necessary to change the problematic behavior. Coping skills involve both cognitive (i.e., related to motivation and self-efficacy) and behavioral (i.e., action-oriented) strategies. For example, "urge surfing" involves noticing but not resisting urges to engage in pre-change behavior, as these urges will wax and wane (like an ocean wave). By not resisting the urge this does not mean giving in to the urge and engaging in pre-change behavior. Often times attempts to resist the urge will make the client feel the urge more intensely for a longer period of time. Mindfulness meditation also identifies a coping strategy of "staying in the moment" and becoming thoughtfully aware of urges and cravings without reacting to them.

Increasing self-efficacy (i.e., beliefs about one's ability to influence the events that affect one's life) is associated with a person's ability to cope in high-risk situations. Low self-efficacy may be a mediating factor in lapse or relapse. Following the identification of high-risk situations and successful implementation of coping strategies, self-efficacy may increase regarding one's ability to maintain the positive behavioral change. For example, after becoming anxious (a high-risk situation), an individual may employ a new coping strategy by applying relaxation techniques; the person may then notice a decrease in anxiety without substance use. The person's self-confidence in applying new techniques and avoiding problematic behaviors is thereby increased.

RP also addresses ambivalence, which can undermine behavior change and maintenance. RP attempts to shift the focus from immediate desires (e.g. "drinking with my friends will be fun tonight") to long-term goals and values (e.g., "although I may have fun tonight, having a hangover would get in the way of studying, and my grades are starting to slip"). Finally, RP considers the importance that social support has in the long-term maintenance of behavior change. RP seeks to integrate additional interventions, including marital counseling, involvement in social organizations, and enhancement of existing supportive relationships.

The process of changing one's habits is not always a binary condition (use/don't use, drink/don't drink), and RP cannot be considered in simplistic terms either. When a commitment for change has been achieved, it is critical to address all the conditions that may result in relapse and undermine success. The dynamic model of RP provides a foundation for supporting these positive changes.

See also **Relapse; Treatment, Behavioral Approaches to: Overview; Treatment, Stages/Phases of: Aftercare.**

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STABILIZATION

Various evidence-based pharmacological and psychosocial interventions are relevant to different stages in the addiction career and treatment process (UNODC, 2008). Stabilization is a fundamental concept woven into these programs and can refer to several processes. A stabilizing period is generally meant to provide a safe, secure environment in which to engage the patient and develop a treatment plan that he or she will follow after discharge.

The first step in treatment is often detoxifying the patient. This phase includes a brief stabilization period designed to detoxify the patient from addictive drugs, to assess his or her psychosocial stability, and to begin to establish basic recovery supports. This process might include medical detoxification, in which the client is systematically withdrawn from drugs that produce physical dependence, typically under the care of a physician and through the use of medications that reduce the risks to the patient and/or increase the patient's comfort. The primary goals of this phase include stabilizing the acute symptoms of the drug use disorder, helping the patient establish abstinence, and motivating the patient to continue in treatment once the acute crisis has subsided or the involuntary period of commitment expires. This phase can last as long as two weeks, after which patients usually start individual or group treatment and move toward a period of more stable abstinence. Stabilization is usually indicated by a significant period of abstinence, a safe and consistent housing situation, adequate levels of social support, and the absence of acute or unstable medical or legal problems.

For patients with opioid dependence, maintenance medications such as methadone or buprenorphine have proven efficacy in stabilization and relapse prevention. Although these drugs themselves can produce physical dependence, they serve to stabilize and reduce illicit opioid abuse by these patients, making them more receptive to other forms of intervention.

Social assistance and support are often also needed. To achieve sustainable livelihoods, addicted patients who are unemployed, homeless, and/or rejected by their families benefit from programs such as dormitories, vouchers, and temporary job opportunities. These support the patients' stabilization when offered in combination with social services and treatment services.

For many people, alcohol and drug abuse have characteristics of chronic disorders, with recurring cycles of cessation and relapse. Similarly, many drug users go through cycles of treatment, abstinence, and relapse (Hser et al., 1997). McKay (2005) emphasized this cyclic nature of treatment and the importance of establishing stabilization each time. He writes that methods need to be developed to increase patients' willingness to return to more intensive forms of treatment as needed until stabilization is achieved once again.

See also **Treatment, Stages/Phases of: Initiation of Abstinence; Treatment, Stages/Phases of: Relapse Prevention.**

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AFTERCARE

The recovery process does not end when an individual completes a detoxification, rehabilitation, or stabilization program. Due to the relapsing nature of substance abuse, individuals receiving treatment for the disorder are generally urged to participate in some form of continuing care after their initial phase of treatment has ended (McKay et al., 2004). In the realm of substance abuse treatment, the terms *continuing care* and *aftercare* have similar, yet distinct, meanings.

Substance abuse treatment used to be delivered primarily in inpatient or residential settings, and patients would participate in aftercare group therapy sessions near the end of their treatment stay. These aftercare sessions were intended to maintain the progress achieved in the inpatient/residential

program by easing the transition from the controlled therapeutic environment to one in which alcohol and drugs are readily available.

As of 2008, in the United States, most substance abuse treatment is provided in outpatient settings, with residential or inpatient treatment restricted to those with severe comorbid medical or psychiatric problems (McKay, 2005). The continuing care phase in the outpatient model is typically delivered in group sessions, focuses on substance use, and is often structured like twelve-steps mutual/self-help programs.

Differences exist between the role of continuing care in outpatient programs and aftercare programs from the old residential service delivery model. In contrast with the inpatient model, most graduates of an outpatient treatment program have already demonstrated some ability to achieve and maintain abstinence outside a controlled environment (McKay et al., 2004). While maintaining abstinence is paramount for these individuals, some researchers argue that continuing care should also include other components of recovery, such as focus on improving the individual's social support system and making use of recovery houses. These researchers assert the need for vocationally- and activities-focused skills-training programs (Donovan, 1998).

Aftercare also plays an important role in drug treatment programs within U.S. prisons, although the evidence for its effectiveness continued to be evaluated in the early twenty-first century. In awarding residential substance abuse treatment grants for state prisoners, the Bureau of Justice Assistance requires states to give preference to programs that provide aftercare services. Also, the standard of care established by the Office of National Drug Control Policy specifies that community-based aftercare must continue for at least six months. In addition to this emphasis on aftercare, researchers emphasize the need to understand better how different criminal justice systems conceptualize and implement these programs. Standard definitions and procedures are needed to determine the level and intensity of services required for different types of offenders in various types of settings (Pelissiera et al., 2007).

Given that long-term programs are expensive, it makes sense to select candidates who will be best served by them. Research shows that some individuals with substance use disorders recover without formal treatment (Sobell et al., 1993) and that others experience durable improvements following such brief interventions as motivational interviewing. Individuals who are unable to achieve sustained reductions in alcohol or drug use either on their own or following brief interventions may be the best candidates for extended interventions (McKay, 2005).

See also **Methadone Maintenance Programs; Relapse.**

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TREATMENT: OUTPATIENT VERSUS INPATIENT SETTING. The marketplace for treatment for substance use disorders (often referred to as SUDs) offers a range of options from which to choose. These options are commonly classified as either *inpatient* or *outpatient* treatment. Selecting treatment is based on matching an individual's care needs with the necessary supports and an appropriate level of treatment intensity. Although many frameworks exist for describing the variety of treatment options along a continuum of care, the levels of care framework provided by the American Society of Addiction Medicine (ASAM) is one of the most widely used; it is

helpful for describing and differentiating between inpatient and outpatient treatments, as reported by the Center for Substance Abuse Treatment (1994).

INPATIENT TREATMENT

Inpatient treatment generally refers to treatment that is provided in a controlled environment, such as a residential center or hospital. Patients remain in these settings until they are deemed to be ready for treatment in an outpatient setting. Patients with significant withdrawal symptoms, serious medical conditions, suicidal or homicidal ideation, and an inability to function in the community, or those who reside in highly disruptive and unsupportive environments, may benefit most from inpatient treatment (Fuller & Hiller-Sturmhofel, 1999).

The ASAM distinguishes two types of inpatient treatment: medically *managed* and medically *monitored* treatment. Medically managed is the most intensive form of treatment. Because of its high costs, it is typically reserved for persons with acute care needs and severe comorbid conditions (McKay, 2001). Services include ongoing primary care to manage withdrawal symptoms and other psychiatric, medical, and emotional problems associated with substance dependence. This treatment creates a safe environment for detoxification, while allowing clinicians to make differential diagnoses, stabilize symptoms, and develop care management plans.

Medically monitored treatment is also provided in a residential setting but does not include primary medical services. Medically monitored treatments may be provided in private or public treatment centers, as well as state and local psychiatric hospitals. Treatment may last from several days to several weeks. Depending on the specific care needs of the patient, treatment may focus on managing symptoms, developing coping skills, reducing risk of self-harm, improving independent living skills, and establishing supportive social networks (see Daley & Salloum, 2001).

OUTPATIENT TREATMENT

Outpatient treatment involves nonresidential services and does not include an overnight stay in a hospital or treatment center. This type of treatment allows an individual to receive treatment services while maintaining normal daily activities. Outpatient treatments rely heavily on individual- or group-based psychosocial interventions including (but not limited to) cognitive-behavioral therapy (CBT), motivational enhancement therapy (MET), and psychoeducation. A meta-analysis conducted by Dutra and colleagues (2008) showed that psychosocial interventions for substance use disorders exhibited effect sizes that were comparable to other efficacious treatments in psychiatry. Pharmacological treatment is also considered an important treatment component for many patients in outpatient treatment. Such therapies may be agonist medications (e.g., methadone and buprenorphine for opioid dependence), antagonist medications (e.g., naltrexone for opioid dependence), abstinence- and relapse-preventing medications (e.g., disulfiram, naltrexone, and acamprosate for alcohol dependence; bupropion and varenicline for tobacco dependence), or those used for the treatment of comorbid psychiatric conditions (e.g., antidepressants, antipsychotics, and mood stabilizers) (Work Group on Substance Use Disorders et al. & American Psychiatric Association Steering Committee on Practice Guidelines et al., 2006).

The ASAM recognizes two levels of outpatient treatment: intensive outpatient and standard outpatient. Intensive outpatient treatment is the highest and most comprehensive level of outpatient treatment. Also referred to as partial hospitalization, it is considered a *step-down* from inpatient services. This treatment option bridges inpatient and outpatient services, offering daily treatment groups and professional contacts while allowing patients to return to their primary residence rather than stay overnight in a hospital. Intensive outpatient treatment may last a few days to a few weeks. Standard outpatient treatment differs in intensity and duration from intensive inpatient treatment and is offered in a variety of settings that range from community mental health centers to patient-driven support groups. Depending on the care needs of the patient, standard outpatient treatment may involve a few treatment sessions a month or multiple sessions each week.

Other outpatient treatment options exist, although they do not fall within the ASAM level of care taxonomy. For example, self-help groups, such as Alcoholics Anonymous (AA), Narcotics Anonymous (NA), and other 12-step models, are outpatient treatments that may constitute a person's primary form of treatment, may be an

adjunct to existing professional services, or may be a way of providing additional support following intensive treatment, also referred to as aftercare. For example, Gossop and coworkers (2008) reported that attending AA or NA meetings after receiving inpatient services was associated with higher levels of abstinence for opioids and alcohol at one, two, and five years follow-up compared to those who did not attend AA or NA, or who attended infrequently.

Brief interventions delivered by health service providers from numerous disciplines are another type of treatment. These are structured interventions of short duration—typically 5 to 30 minutes—designed to help people think differently about their level of substance use. They have been shown to reduce substance misuse, particularly alcohol consumption, and are cost-effective. Brief interventions can also serve to enhance a person's motivation to participate in formal treatment services. In addition to reducing substance use, brief interventions have also been found to reduce utilization of health-care services (e.g., Fleming, Barry, Manwell, et al., 1997).

Case management is another form of treatment for substance use disorders. This type of treatment does not directly target the substance use disorder. Instead, it helps address many of the commonly co-occurring psychosocial, psychiatric, and medical problems associated with substance use disorders that interfere with treatment. For example, case management for a patient with limited resources and lacking health insurance may seek to connect this individual with existing public support programs, as suggested by the Center for Substance Abuse Treatment (1998). There is growing evidence of the utility of case management. A series of randomized, controlled trials demonstrated the significant positive effects of case management on measures of substance use, employment, quality of life, psychological functioning, and service utilization (Vanderplasschen, Wolf, Rapp, et al., 2007; see also Saleh et al., 2002).

CONCLUSIONS

Although various frameworks exist to describe the continuum of care options for treating substance use disorders, no framework fully captures the significant heterogeneity that exists within the various types of inpatient and outpatient treatment options. For example, these different types of services may have differing theoretical orientations, terms of attendance, completion requirements, physical settings, and staff training requirements. Moreover, although the framework can help guide the selection of treatments, other factors also determine where an individual receives treatment. This includes, but is not limited to, the availability of services, connection with the criminal justice or psychiatric system of care, cultural compatibility of services, and funding.

It is also important to consider how these service types will continue to change in the future. In the early twenty-first century inpatient services remain the treatment of choice for severe and acute conditions; however, to reduce cost and increase access for underserved populations, many efforts are being made to adapt inpatient services to outpatient settings. Across all types of treatment options, additional research is needed to identify the key ingredients of treatment and determine how treatments can be better tailored for comorbid conditions. Research is also needed to understand better how treatments can be adapted for at-risk populations, such as minorities, women, and adolescents, as advanced by Ashley, Marsden, and Brady (2003).

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TREATMENT ACCOUNTABILITY FOR SAFER COMMUNITIES (TASC). Developed in 1972, the Treatment Accountability for Safer Communities (TASC) was created by President Richard M. Nixon's Special Action Office for Drug Abuse Prevention (SAODAP) and funded by the Law Enforcement Assistance Administration (LEAA) and the National Institute of Mental Health (NIMH). The acronym originally stood for "Treatment Alternatives to Street Crime," reflecting the original emphasis of the program. Since its inception, TASC has provided leadership and advocacy to foster and improve the integrated delivery of substance abuse treatment to nonviolent offenders. The first TASC programs under SAODAP were operational in Wilmington, Delaware, and Philadelphia, Pennsylvania.

In the mid-1990s, TASC programs received support from the U.S. Department of Justice through the Bureau of Justice Assistance (BJA) Criminal Justice Block Grants, which are given to state and local governments. (LEAA was discontinued in 1982.) Many TASC programs have expanded their base of support so that state and federal funding is supplemented by private donations and grants or client fees. In 2008 TASC was operating in more than 100 jurisdictions in 28 of the U.S. states and territories. National TASC provides membership association and represents over 220 programs across the United States. The programs supported by National TASC are dedicated to the professional delivery of assessment and case management services to substance-involved individuals in the criminal justice and court systems. TASC has a large presence in some states, such as Florida, New York, North Carolina, Ohio, Pennsylvania, Illinois, Arizona, and Colorado.

Since the 1970s, TASC has evolved from providing the infrastructure to manage clients throughout the criminal justice system and supporting both justice and treatment independently to working in conjunction with drug courts, reentry management programs, and other efforts. The idea for the initial TASC programs derived from an analysis of the criminal justice system that indicated that many drug-addicted arrestees were released on bail while awaiting trial, and that these individuals were likely to continue to commit crimes. Although there were provisions for supervision of drug-dependent offenders after conviction (through probation) or after release from prison (through parole), no such mechanisms were in place to provide supervision of those awaiting trial. It was felt that if these arrestees could be directed to treatment, any success in treatment could be taken into consideration at the time of trial.

In addition to being an effective program model, TASC has also brought together the critical elements fundamental to integrating the criminal justice and substance abuse treatment systems. Both of these systems, as well as the offenders, are held accountable through the implementation of client-specific case

management. TASC methods can be utilized by programs or systems attempting to manage drug-involved offenders. Because it is a methodology as well as a program model, TASC methods are applicable for moving offenders through a range of sentencing options—from deferred prosecution or pretrial release through incarceration and probation or parole, as well as residential and nonresidential treatment programs and aftercare. TASC methodology is essential to developing the partnerships between the justice system and the treatment delivery system that characterize many successful offender management programs, including drug courts and Breaking the Cycle programs. Between 1997 and 2001, Breaking the Cycle demonstration programs tested the feasibility and impact of system-wide intervention to reduce drug use among offenders by identifying and intervening with drug-involved felony defendants.

The TASC approach is to engage addicted offenders referred by criminal justice officials in substance abuse treatment and other ancillary services that address the needs of this population. The goal of TASC programs is to provide a treatment intervention that can stop the cycle of addiction, arrest, incarceration, and release. This is achieved through a specialized system of clinical case management that encourages positive behavior change and long-term recovery for individuals in criminal justice, corrections, juvenile justice, child welfare, and public aid settings. The purpose of the TASC program is to ensure that underserved populations gain access to the services they need for health and self-sufficiency, while also ensuring that public and private resources are used most efficiently.

In addition, TASC seeks to:

1. Serve as a vehicle for coordinating decision making and programming related to substance involved justice populations.
2. Offer information and education to both treatment providers and the justice system.
3. Provide practitioners with effective strategies for managing this population.
4. Participate and serve on boards and other entities that determine policies and procedures regarding the delivery of services.
5. Facilitate activities and events that encourage collaboration.

To standardize TASC as an effective national model for dealing with substance-abusing offenders, the U.S. Department of Health and Human Services developed guidelines for jurisdictions to operate an effective TASC program. The guidelines developed reflect those methods that can best identify eligible candidates, address critical service gaps, improve program management, and enhance service delivery standards. The guidelines incorporate 13 elements that are divided into three sections: (1) systems coordination, (2) organization, and (3) operation. The two systems coordination elements help provide the overarching support from the criminal justice, treatment, and other social services systems needed to manage addicted offenders effectively. The five organizational elements attempt to build the structural foundation necessary for TASC programs to provide client services that support the larger systems. The six operational elements delineate the minimum set of client activities that are performed by the TASC organization on an ongoing basis.

TASC procedures determine a drug-dependent offender's eligibility for intervention. These include an assessment of the offender's risk to the community, severity of drug dependence, and appropriateness for treatment placement. After an individual is referred to a treatment program, TASC case-management services monitor that individual's compliance with the conditions of the treatment and rehabilitation regime, including expectations for abstinence, employment, and improved personal and social functioning. Progress is reported to the referring justice-system agency. Clients who violate the conditions of their justice mandate—the TASC "contract," or treatment agreement—are usually returned to the justice system, where the legal process interrupted by the TASC diversion goes forward.

TASC programs play an important role in reducing the growing rates of drug-related street crime and alleviating court backlogs. They have been effective in identifying drug-involved offenders in need of treatment, assessing the nature and extent of their drug use and their specific treatment needs, and referring them to treatment. TASC clients have been found to remain in treatment longer and have better posttreatment success than those offenders who do not participate in the program. In addition, as an adjunct to parole and work release, TASC programs have the potential to help ease prison

overcrowding. TASC also effectively fulfills its original purpose of linking the criminal justice system and the treatment system by providing client identification and monitoring services for the courts, probation departments, and other segments of the criminal justice system.

See also **Civil Commitment; Civil Remedies; Coerced Treatment for Substance Offenders; Crime and Drugs; Criminal Justice System, Treatment in the; Narcotic Addict Rehabilitation Act (NARA); U.S. Government Agencies: National Institute on Drug Abuse (NIDA).**

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TREATMENT OUTCOME PROSPECTIVE STUDY (TOPS). This entry reports the results of a clinical, epidemiological study of clients who entered drug-abuse treatment programs from 1979 to 1981. During the course of the Treatment Outcome Prospective Study (TOPS), 11,182 clients were interviewed at admission to drug-abuse treatment by program researchers hired to work in assigned clinics and professionally trained, and supervised by Research Triangle Institute (RTI) field staff. The interviews at admission covered demographics; history of drug use, treatment, arrest, and employment in the year prior to treatment; and status upon admission to treatment. The National Institute on Drug Abuse (NIDA) and RTI cosponsored the study. The population under study included 4,184 clients from 12 outpatient methadone programs, 2,891 clients from 14 residential programs, and 2,914 clients from 11 outpatient drug-free programs in 10 cities. Program researchers collected the responses to questions on behavior, services received, and satisfaction posed during interviews conducted every three months while clients remained in treatment. The self-report data were supplemented with data abstracted from the clinical and medical records of all clients selected for follow-up, and counselors and program directors completed questionnaires describing the treatment philosophy, structure, practice, and process.

The follow-up data included interviews 1 and 2 years after treatment with 1,130 clients who had been admitted in 1979; follow-ups 90 days and 1 year after treatment of 2,300 clients who had entered treatment in 1980; and follow-ups 3 to 5 years after treatment of 1,000 clients who had entered programs in 1981. Professional field interviewers hired, trained, and supervised by RTI field staff were able to locate and interview between 70 and 80 percent of the clients selected for these interviews.

TOPS resulted in a substantial body of important knowledge about drug-abuse treatment and its effectiveness. The client populations of outpatient methadone programs, long-term residential programs, and outpatient drug-free programs who participated in TOPS differed on many sociodemographic and background characteristics. Residential clients were significantly more likely to report the multiple use of drugs, drug-related problems, suicidal thoughts and attempts, heavy drinking, predatory crimes, and less full-time employment compared to methadone clients. Outpatient drug-free clients were more likely than methadone clients to report drug-related problems, suicidal thoughts or attempts, predatory crimes, and heavy drinking, but were less likely than residential clients to use multiple drugs. These results demonstrated that each type of program served very different, important segments of the drug-abusing population. The high rates of self-referrals to methadone treatment (48%) and criminal justice referrals to residential

and outpatient drug-free treatment (31%) suggest differences in clients' motivations for seeking treatment and, consequently, differences in retention, services received, and outcomes.

The drug-abuse patterns reveal the differential concentration of types of drug abusers across major categories. Clients on methadone were primarily (52%) traditional heroin users who used only cocaine, marijuana, and alcohol in addition to heroin. One in five of these clients, however, used heroin and other narcotics, as well as a variety of non-narcotic drugs. The remaining twenty-five percent of clients on methadone were classified as former daily users who had a history of regular use but did not use heroin on a weekly or daily basis in the year prior to treatment. Residential clients had diverse patterns of use, and the majority of outpatient drug-free clients were users of alcohol and marijuana (36%) or single non-narcotics users (22%).

Symptoms of depression are very commonly reported by clients entering drug-abuse treatment programs. Overall, about 60 percent of TOPS clients reported at least one of three symptoms of depression at intake. Nearly 75 percent of the women under 21 years of age reported one or more symptoms of depression. Other results suggest that the duration of regular drug use and the number of prior treatment episodes are important indicators of the effectiveness of any single treatment episode; clients with lengthy drug-abuse or drug-treatment histories have poorer prognoses.

Clients who have come into treatment by way of the criminal justice system do as well or better than other clients in drug-abuse treatment. Formal or informal mechanisms of the criminal justice system appear to refer individuals who had not been treated previously and many who were not yet heavily involved in drug use. Involvement with the criminal justice system also helps retain clients in treatment up to an estimated six to seven additional weeks. Drug-abuse treatment programs vary in the nature and intensity of the treatment services provided, the types of therapists and therapies provided, the average length of stay, and the inclusion or exclusion of aftercare.

The study of the treatment process in TOPS programs focused on many important aspects of the structure, nature, duration, and intensity of drug-abuse treatment. Descriptions of aspects of the treatment process were developed from clients' self-reports of the need for treatment services, services received, and satisfaction, combined with abstractions of clinical and medical records and descriptions of programs by counselors and directors. The outpatient methadone and outpatient drug-free treatment programs had budgets per slot of approximately $2,000. U.S. therapeutic communities expended an average of $6,135 per bed.

The number of available services (medical, psychological, family, legal, educational, vocational, and financial services) varied during the years 1979 to 1981. Fewer services appeared to be available in the later years of the study. The proportion of clients in residential treatment programs who received family, educational, and vocational services decreased noticeably during the three-year period. During this same period, the clients' demands for services increased. Programs in TOPS appeared to focus on a client's primary drug of abuse rather than addressing his or her multiple drug use, drug-related problems, and social and economic functioning. Low-dose methadone (69% of the clients admitted were initially treated with less than 30 milligrams of oral methadone daily) was the most common pattern of methadone treatment in the programs participating in TOPS.

In TOPS multiple measures of treatment outcome were necessary to describe changes in the client's ability to function in society after treatment. In general, clients who remained in treatment at least 3 months had more positive post-treatment outcomes, but the major changes in behavior were seen only in those who remained in treatment for more than 12 months. Analyses of the TOPS data show that the posttreatment rate of daily heroin, cocaine, and psychotherapeutic-agent use among clients who spent at least 3 months in treatment was half that of the pretreatment rate. The post-treatment rates of weekly or more frequent use for clients who stayed in treatment at least 3 months were 10 to 15 percent lower than the rates for shorter-term clients. The results showed that time spent in treatment was among the most important predictors of positive treatment outcomes. Stays of one year or more in residential or methadone treatment, or continuing maintenance with methadone, produced significant decreases in

the odds of a client using heroin in the follow-up period. Clients in TOPS also reported a substantial decrease in the symptoms of depression during the years after treatment.

Analyses of the effects of treatment on behavior have focused on reductions in predatory crime and the costs associated with crime. The assessment of the cost-benefit ratio indicates that substantial benefits are obtained in reductions of crime-related costs regardless of the measures used within the year after treatment. Reducing transmission of the acquired immunodeficiency syndrome (AIDS) virus would increase the benefit portion of the cost-benefit ratio even further.

See also **Drug Abuse Treatment Outcome Studies (DATOS); Treatment Accountability for Safer Communities (TASC).**

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UNITED KINGDOM: ALCOHOL AND TOBACCO USE AND POLICY.

See **Britain; Britain: Alcohol Use and Policy; Britain: Tobacco Use and Policy.**

U.S. GOVERNMENT

This entry includes the following essays:

THE ORGANIZATION OF U.S. DRUG POLICY

Reducing drug abuse became a priority for the U.S. government in the late 1960s, with continuing expansion of management attention and federal budgets thereafter. In 1969, eight agencies and four cabinet departments received drug-program funding; in 1975, seven cabinet departments were included; the federal drug control program for 2008 involved eleven cabinet departments. In 1969, the total budget for federal drug-abuse programs was $81 million; for 2008, the president's requested budget was approximately $14.1 billion (National Drug Control Strategy, 2008).

Illegal drug trafficking and use present complicated social and law enforcement challenges. The federal government has responded to these challenges in the four decades since the 1960s with increasing governmental agencies and laws. Executive and legislative response has varied over several administrations as the national problems presented by illegal drugs have developed. Drug prevention policy issues are as complex as the illegal drugs they aim to control. This entry explains the development of federal response to the complicated social and legal issues associated with illegal drug trafficking and use.

DIFFICULTIES IN ORGANIZING DRUG POLICY

Illegal drugs come from both international and domestic sources; they include a wide variety of substances; they involve many different forms of transportation, geographical areas, criminal activities, use patterns, and social effects. All these elements are dynamic and constantly adjust to changes in availability of substances and the demand for them. Drug traffickers and active drug users react quickly to drug law enforcement pressures by shifting to areas or techniques that have less risk.

Positive social and legal responses to the illegal drug activity includes all efforts to increase public understanding about the effects of illegal drugs; to develop and increase community-, school-, and family-based programs to reduce drug use; and to promote effective treatment, rehabilitation, and counseling methods. These efforts often require the development and dissemination of new knowledge. They also require evolution of effective laws, development of official roles, and the creation of

agencies and other institutions with diverse agendas and sometimes conflicting interests.

The challenge to federal managers and policymakers is to understand the complex and ever-changing factors that define illegal trafficking and drug use in the United States, and to adjust and adapt the federal response in a timely and effective manner. The executive and legislative branches of government, along with cabinet departments and other governmental agencies, attempt to handle the illegal drug problems at the same time that they work to resolve interdepartmental differences of opinion.

The organization of the federal government is not designed to respond specifically or exclusively to criminal drug activity. There is no cabinet department with line authority over all drug-program resources, and as of 2008 only a few federal agencies are organized around a single drug-related function (e.g., the Drug Enforcement Administration, National Institute on Drug Abuse, and the Substance Abuse and Mental Health Services Administration). All departments have other, often overarching, roles, so they must balance their drug and non-drug responsibilities. Indeed, every step in the policy-determination and -implementation process is subject to bureaucratic, political, and technical differences of opinion. Two challenges in addressing the drug problem are: (1) reaching agreement on the extent and nature of the problem, and (2) assessing the impact of the federal effort on the ever changing nexus of factors. To overcome these and other difficulties, between the early 1970s and the early 2000s, the federal organization for determining drug policy and implementing drug programs expanded in both scope and effort. As of 2008, eleven federal departments were involved in drug prevention efforts (*2008 National Drug Control Strategy*).

HISTORY

A chronological summary of drug-policy coordinating mechanisms is presented below, beginning with 1971, first from the perspective of the Executive Branch and then from the perspective of the Legislative Branch.

Executive Drug Policy (1971–1976). President Richard M. Nixon created the Special Action Office for Drug Abuse Prevention (SAODAP) in the Executive Office of the President (EOP) in June 1971, which was designed to lead and coordinate all federal drug-abuse prevention activities. The first director, Jerome H. Jaffe, also served as consultant to the president for narcotics and dangerous drugs. SAODAP monitored the annual budget and prepared budget analyses of all federal drug-abuse programs, by agency and by activity.

After the 1971 creation of SAODAP, there was a continuous presence in the White House structure of a federal drug coordinating and management effort. Thus, the federal responders to criminal drug activity had a special pleading office for these social issues with a consistent presence in the White House, which is most unusual.

Also in 1971, President Nixon called for "an all out global war on the international drug traffic" (*1973 Federal Strategy*, p. 112). His organization for policy incorporated an international perspective. International efforts were coordinated by the Cabinet Committee on International Narcotics Control (CCINC), chaired by the secretary of state. Established in August 1971, CCINC was responsible for developing a strategy to stop the flow of illegal narcotics into the United States and for coordinating federal efforts to implement that strategy. Domestic drug-law enforcement had a high priority within the normal cabinet-management system.

In January 1972, President Nixon created the Office of Drug Abuse Law Enforcement (ODALE) in the Department of Justice (DOJ) and gave the ODALE director, Myles J. Ambrose, the added title of consultant to the president for drug abuse law enforcement. The directors of both SAODAP and ODALE had a policy oversight role in advising the president.

The 1972 legislation authorizing SAODAP also created the Strategy Council on Drug Abuse (known as the Strategy Council) and directed the "development and promulgation of a comprehensive, coordinated, long-term Federal strategy for all drug abuse prevention and drug traffic functions conducted, sponsored, or supported by the Federal government." The cabinet-level Strategy Council, with the directors of SAODAP and ODALE as co-chairmen, prepared the *1973 Federal Strategy for Prevention of Drug Abuse and Drug Trafficking*, the first explicit drug-prevention strategy document.

Additional federal strategies were published in 1974 and 1975 during the directorship of Robert L. DuPont, establishing the precedent for the over 25 similar strategies that were subsequently published, and as of 2008 remained an important product of the federal drug-prevention policy effort.

In 1975, SAODAP was phased out under a sunset provision in its enabling legislation. Program initiatives in research, prevention, treatment, and rehabilitation were transferred to the newly established national Institute on Drug Abuse (NIDA), and SAODAP director DuPont became the founding director of NIDA. Responsibility for federal drug prevention coordination fell to the office of Federal Drug Management (FDM), within the Office of Management and Budget (OMB), which supported senior officials of OMB, the CCINC, and the White House Domestic Council.

In early 1975, President Gerald R. Ford directed the White House Domestic Council to review the federal drug effort. Vice President Nelson A. Rockefeller chaired the interagency Domestic Council Drug Abuse Task Force, with the chief of FDM as study director. The task force, with advice from community organizations, prepared the comprehensive *1975 White Paper on Drug Abuse*. This report recommended assigning responsibility for overall policy guidance to the Strategy Council on Drug Abuse; creating an EOP Cabinet Committee to coordinate prevention and treatment activities; and continuing a small staff in OMB to assist the Strategy Council and the EOP. In April 1976, President Ford announced two new cabinet committees, the Cabinet Committee on Drug Law Enforcement and the Cabinet Committee on Drug Abuse Prevention "to ensure the coordination of all government resources which bear on the problem of drug abuse" (*Federal strategy: Drug abuse prevention,* 1976, p. 26). The cabinet committee structure, supported by the FDM staff, worked to the satisfaction of President Ford but did not satisfy Congress.

Congress enacted legislation establishing an Office of Drug Abuse Policy (ODAP) in March 1976, seeking a single individual in the EOP with responsibility for the overall drug program. President Ford did not activate the new agency, however, but chose to continue with the three cabinet committees, supported by the FDM staff.

Executive Drug Policy (1977–1980). In March 1977, President Jimmy Carter revised the drug-policy structure, activating ODAP and abolishing the three drug-related cabinet committees. He also revitalized the Strategy Council, with the director of ODAP as executive director, to serve as the government-wide advisory committee for all drug-abuse matters. ODAP worked particularly well with the White House staff, partially because Director Peter Bourne was also special assistant to the president for health issues and had an excellent relationship with President Carter and the White House staff. ODAP aggressively pursued a wide range of policy and coordination activities, including a major review of all federal drug programs.

The President's Reorganization Project reviewed the organization of the Executive Branch and recommended abolishing ODAP in mid-1977. Within the EOP, ODAP was an unusual federal agency, with a strong presence and authority for a single issue, somewhat atypical in the EOP structure. Thus, ODAP was a logical target in efforts to streamline the EOP. Congress disagreed strongly with the elimination of ODAP, however. After congressional hearings and negotiations, the Carter administration compromised by continuing part of the ODAP staff and all the ODAP functions as part of the White House Domestic Policy Staff (DPS).

In March 1978, six members of the ODAP staff were transferred to DPS and became the Drug Policy Office (DPO). The DPO continued to perform ODAP functions, including responding to congressional interests and reporting directly to Peter Bourne. After Bourne departed the White House staff in 1978, the drug staff worked through the DPS director. In May 1979, the president affirmed the head of DPO, Lee Dogoloff, as the individual primarily responsible for federal drug-abuse prevention and control programs. DPO published the *1979 Federal Strategy* and the *1980 Annual Report*. A major policy-coordinating mechanism was the monthly meetings held by DPO with the heads of the major operating agencies (called the Principals Group). DPO also supported the National Narcotics Intelligence Consumers Committee, another policy-coordinating mechanism, which was established in April 1978, and it initiated efforts to increase military support for drug-interdiction activities.

Executive Drug Policy (1981–1988). In 1981, President Ronald Reagan's Office of Policy Development (OPD) included a Drug Abuse Policy Office (DAPO) similar in organization and role to the preceding DPO. President Reagan charged DAPO with (1) a full range of policy-development and coordination activities, (2) international negotiations, and (3) assisting the drug-abuse prevention efforts of First Lady Nancy Reagan. In addition to overseeing the efforts of the federal drug agencies, DAPO emphasized the use of all opportunities for the federal government to encourage a wide range of non-government anti-drug activities. DAPO was directed by Carleton Turner, a pharmacologist, who was succeeded in 1987 by Donald Ian MacDonald, a pediatrician. DAPO published the *1982 Federal Strategy*, and reflecting the subsequent broader policy direction, in 1984 it published the *National Strategy for Prevention of Drug Abuse and Drug Trafficking*.

DAPO continued the coordination meetings with the agency heads (the previous Principals Group, renamed the Oversight Working Group) and assisted in the design and implementation of the National Narcotics Border Interdiction System (NNBIS), headed by Vice President George H. Bush. DPO assisted the Cabinet Council on Legal Policy and the Cabinet Council on Human Resources with drug matters until the cabinet councils were replaced by the Domestic Policy Council in April 1985. The Domestic Policy Council Working Group on Drug Abuse Policy prepared a major presidential drug initiative in 1986, with assistance from DAPO.

During the 1980s, the oversight of drug law enforcement moved away from the White House. In 1984, Congress had established a federal drug law-enforcement czar to "facilitate coordination of U.S. operations and policy on illegal drug law enforcement." The attorney general was chairman of the new cabinet-level National Drug Enforcement Policy Board (NDEPB) with staff offices in the Department of Justice. DAPO was charged with ensuring "coordination between the NDEPB and the health issues associated with drug abuse," in addition to supporting the president and the White House staff. In January 1987, the NDEPB published the *National and International Drug Law Enforcement Strategy*, which expanded on the sections of the *1984 National Strategy* pertaining to drug law enforcement and international controls. DAPO continued to provide Executive Office oversight of the entire drug program.

In 1987, President Reagan replaced the NDEPB by creating the National Drug Policy Board (NDPB) to coordinate all drug-abuse policy functions. The director of the White House DAPO was a member and assisted the NDPB in developing health-related drug policy. The NDPB published *Toward a Drug-Free America—The National Drug Strategy and Implementation Plans* in 1988.

In late 1988, Congress again passed drug czar legislation, authorizing a new agency named the Office of National Drug Control Policy (ONDCP) in the EOP.

Executive Drug Policy (1989–2000). ONDCP began operation in the EOP in early 1989, absorbing the NDPB and terminating the two existing White House drug activities, DAPO and NNBIS. Although never actually a member of the cabinet, the first two cabinet-level directors were given broad responsibilities for developing and guiding the National Drug Control Program, including developing an annual strategy and overseeing its implementation. The first director, William Bennett, had been secretary of education in the Reagan administration; he was succeeded by Robert Martinez, a former governor of Florida. ONDCP had oversight of organization, management, budget, and personnel allocations of all departments and agencies engaged in drug control activities. ONDCP used a complex set of interagency coordinating committees under a Supply Reduction Working Group, a Demand Reduction Working Group, and a Research and Development Committee. The director chaired the NSC Policy Coordinating Committee for Narcotics, which ensured coordination between drug law enforcement and national security activities. The director also provided administrative support to the President's Drug Advisory Council, which in turn assisted ONDCP in supporting national drug-control objectives through private sector initiatives. ONDCP was required to establish realistic and attainable goals for the following two years and the following ten years and to monitor progress toward the goals. Following the election of President Bill Clinton, Lee Brown, a criminologist

and former New York police commissioner, was appointed director of ONDCP and was also given membership in the cabinet. The fourth director, retired U.S. Army General Barry R. McCaffrey, was appointed in 1996 and served until 2001.

Executive Drug Policy (2001–2008). Strong drug policy national leadership characterized the Bush White House in the years from 2001 through 2008. During this period, while law enforcement efforts remained robust, more White House attention was given to primary prevention issues, especially school-based drug prevention efforts that included random drug testing. In addition, ONDCP increasingly reached out to state and local stakeholders. John Walters served as drug czar from 2001 into 2008, a period of unprecedented stability and consistent policy leadership.

Beginning in 2002, the National Drug Control Strategy included specific goals. That year, it was announced that the strategy would pursue ambitious goals: a 10 percent reduction in youth drug use in two years, and a 25 percent reduction in youth drug use over five years. This action constituted one of the first instances in which specific goals were established for the reduction of drug use in the United States. Each successive strategy tracked these goals. The 2005 and 2008 strategies cited other surveys and other data that indicated decreases consistent with these goals. The goals were restated in 2008 for an additional 10 percent reduction in youth drug use in 2008, using 2006 as the baseline.

The *2008 Strategy* had three main initiatives. The first initiative was aimed at preventing drug use through the development and implementation of community efforts designed to change attitudes. These efforts included school-based random testing, combating doping in sports, promoting drug-free programs, and developing community-based programs to support a drug-free society. A national antidrug media campaign supported efforts to educate youth about the dangers of drug use and encourages states to use federal block grant money to promote local efforts.

The second initiative was designed to improve nationwide efforts to effectively identify and treat people who have drug problems, including between screening to detect drug use, effective measures of intervention, medical education initiatives, and advances in treatment regimens. These efforts were supported by the continued promotion of drug courts, which serve as important referral sources, and of family drug treatment courts. Also promoted were new approaches to treating co-occurring disorders because many people entering drug treatment programs have other medical or psychological problems such as schizophrenia and depression. These efforts represented a clear departure from strategy focus at the end of the twentieth century.

The third initiative was to continue a robust effort designed to disrupt the market for illegal drugs at home and abroad. Efforts included increasing the viability and effectiveness of local and state law enforcement in recognition of their growing role in fighting pharmaceutical diversion, closing open-air drug markets, and tackling domestic marijuana cultivation. Border security remained a high priority for reducing the flow of drugs coming into the United States from Mexico, the Caribbean, and South America, and for attacking trafficker finances by improving intelligence and assisting other governments developing their capabilities to interdict couriers through training and technical assistance programs funded by the U.S. Department of State.

BUDGET INDICATORS

The budget is divided into two broad components aimed at reducing the demand for drugs and disrupting their supply. The budgets span five years of the Clinton administration and five years (including one projected based on the 2005 request) of the George W. Bush administration. One administration was Democrat, the other Republican, yet the allocation of funding was similar. Both the highest and lowest percentage of funds allocated to the response side took place during the Clinton administration, the highest in FY 1998 when 50.1 percent of the budget went to treatment and prevention, the lowest in FY 2000, when only 43.2 percent of funds went to stem demand. FY 2000, conversely, also saw the highest allocation of funds to disrupting the supply of drugs, 56.7 percent of the budget. The Bush administration's request for FY 2008 divided funding: 35 percent for demand reduction and 65 percent for disrupting supplies (*2008 National Drug Control Strategy,* p. 4). In the ten years since FY 1998, funds for law enforcement, interdiction, and international programs

were higher than funds allocated to treatment, prevention, and research to support these efforts.

A study of the budget allocations between 1996 and 2005 indicated that funds were divided (unequally) between drug abuse treatment and programs of prevention (*The National Drug Control Strategy—The Federal Drug Budget*). Treatment received 24.5 percent of the total budget during the FY 1996–2005 period, prevention 14.4 percent. In the requested budget for FY 2005, treatment made up 24.4 percent and prevention 12.4 percent, both increases over the previous few years, but still below historic averages over the previous decade.

The study also noted that when the research funding to support these two activities was added, treatment for 29.2 percent of the total budget over the period and 29.4 percent in the 2005 budget request (28.1% enacted in 2004); prevention, with research, averaged 17.6 percent over the ten-year period and received 15.6 percent in the 2005 budget request (16.4% enacted by Congress in FY 2004) (*2008 National Drug Control Strategy,* p. 4). On average, over the ten-year period shown, treatment (with research) received 62.5 percent and prevention (with research) 37.1 percent of the demand-reduction component of the budget. Treatment funds went into actual treatment of individuals, typically through grant programs to states.

During the entire ten-year period supply distribution consumed 53.2 percent of the total federal drug control budget, slightly less than the percentage that it was allocated in the FY 2005 budget request. Within this component, domestic law enforcement was the largest piece (46.6% over the ten-year period). Interdiction came next (36.9%), and international programs were last (16.5%).

As of 2008, most domestic law enforcement funds were spent by the DOJ (or on its behalf) and underwrote the operations of the Drug Enforcement Administration, the chief domestic drug control agency. Interdiction funds were managed by the U.S. Department of Homeland Security (DHS), which as of 2008 oversaw all border control functions and the U.S. Coast Guard. International funds were divided roughly equally between the U.S. State Department and the U.S. Department of Defense. The Department of State's Bureau of International Narcotics and Law Enforcement Affairs was the lead agency managing international programs. The Department of Defense was involved in supporting anti-insurgency programs in the Andean region and elsewhere.

As of 2008, the most budgetary fluctuation over time was associated with international programs. Significant portions of this budget were expended on supporting international eradication efforts that, in turn, depend on the cooperation of other countries and on the U.S. drug certification program, which was able to temporarily deny funding to certain regimes. Funds ranged from 3.9 percent of the total budget (FY 1996) to 15.9 percent (FY 2000); in 2001 funding dropped again to 6.3 percent. The 2008 president's budget request of approximately $1.610 billion comprised just over 11 percent of the president's requested budget.

CONGRESSIONAL DRUG-POLICY OVERSIGHT

Between 1971 and the early 2000s, Congress had a strong and continuing interest in establishing an effective drug-policy oversight mechanism, which would respond to the difficulties of the various committees in attempting to address the drug activities of a single agency within the context of the overall federal effort. Congress was frustrated by repeated failed efforts to establish a drug czar in the EOP to oversee federal drug policy and to advise both the president and Congress.

For example, the Senate Committee on Government Operations had a long-term interest in drug-program oversight and reiterated the programmatic needs for a single, high-level coordinating body with broad statutory authority over federal drug-abuse policy and its implementation. In the House of Representatives, the Select Committee on Narcotics Abuse and Control, headed by Representative Charles Rangel, played an important role in congressional oversight of drug programs and policy. The select committee was formed in July 1976 "to oversee all facets of the Federal narcotics effort and coordinate the response of the seven legislative committees in the House which have jurisdiction over some aspect of the narcotics problem." Without legislative jurisdiction, the select

committee was primarily a fact-finding activity to support the seven standing committees in the House of Representatives. The select committee was also a focal point for congressional pressure for a legislatively based drug czar. In early 1993, Select Committee on Narcotics Abuse and Control was discontinued.

DRUG-POLICY LEGISLATION

In 1972, Congress passed legislation authorizing the Special Action Office for Drug Abuse Prevention, as requested by President Nixon. After SAODAP expired in 1975, Congress authorized a replacement drug-policy agency (ODAP) in early 1976 and was critical of President Ford's decision not to open the new agency.

When President Carter decided to activate ODAP in early 1977, Congress applauded the decision and confirmed the director and deputy director; but ODAP was abolished in early 1978 despite congressional objections, ending the successful relationship between ODAP and Congress. The resulting executive/congressional negotiations required the Drug Policy Office of the DPS to carry out the functions previously assigned to ODAP and to allow congressional access to the drug-policy staff.

In late 1979, Congress followed up with legislation requiring the president to establish a drug-abuse policy coordination system and to designate a single officer to direct the activities (21 USC 1111 & 1112). A system was established by President Carter (Executive Order 12133, 1979, Drug Policy Office) and by President Reagan (Executive Order 12368, 1982, Drug Abuse Policy Office).

In late 1982, Congress enacted a strong drug czar in an Office of National and International Drug Operations and Policy, with a cabinet-level director. The director was granted broad powers to develop, review, implement, and enforce government policy and to direct departments and agencies involved. The explicit power to direct other departments and agencies was seen as too strong and in conflict with the principles of cabinet government. President Reagan did not accept the legislation.

In 1984, the Congress and the administration agreed to establish a cabinet-level NDEPB with a limited charter to coordinate drug law enforcement. The legislation designated the attorney general as chairman and primary adviser to the president and to Congress, on both national and international law enforcement.

In 1987, President Reagan signed Executive Order 12590, broadened the charter of the attorney general and the NDEPB to include the entire federal drug program, and named the new activity the National Drug Policy Board.

In late 1988, Congress passed new drug czar legislation, creating the Office of National Drug Control Policy in the EOP, with a cabinet-level director and funding provisions for both operating expenses and program activities. President George H. W. Bush accepted the new agency and appointed a cabinet-level director, but he did not include the first director or his successor in his immediate cabinet.

Thus, Congress achieved the drug czar objectives that it pursued for two decades: a cabinet-level drug-policy manager with broad oversight of policy and budgets, responsible both to Congress and the president.

WHITE HOUSE DRUG CZARS BY PRESIDENT

Nixon: Jerome H. Jaffe, Robert L. DuPont

Ford: Robert L. DuPont, Edward Johnson (OMB)

Carter: Peter Bourne, Lee I. Dogoloff

Reagan: Ian MacDonald, Carleton Turner

G. H. W. Bush: William J. Bennett, Robert Martinez

Clinton: Lee Brown, Barry McCaffrey

G. W. Bush: John Walters

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; International Drug Supply Systems; Treatment: A History of Treatment in the United States.**

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AGENCIES IN DRUG LAW ENFORCEMENT AND SUPPLY CONTROL

This entry provides an overview of the many federal agencies involved in drug law enforcement and supply control. The Department of Justice serves as the hub for research, crime and law enforcement data, funding for law enforcement efforts, and a significant portion of the law enforcement programs. Other federal agencies playing vital roles in law enforcement efforts are the Office of National Drug Control Strategy, the Department of Homeland Security, the Department of Transportation, the Department of State, the Department of Defense, and the U.S. Postal Service.

DEPARTMENT OF JUSTICE

The Department of Justice (DOJ) was established by the U.S. Congress in 1870 as a part of the Act to Establish the Department of Justice (chap. 150, 16 Stat. 162). The mission of the department is to "enforce the law and defend the interests of the United States according to the law; to ensure public safety against threats foreign and domestic; to provide federal leadership in preventing and controlling crime; to seek just punishment for those guilty of unlawful behavior; and to ensure fair and impartial administration of justice for all Americans." As of 2008, DOJ included fifty-nine executive offices, divisions, bureaus, commissions, and other offices. Approximately sixteen of these offices were actively involved in drug law enforcement and supply control. The Drug Enforcement Administration (DEA); Federal Bureau of Investigation (FBI); Bureau of Alcohol, Tobacco, Firearms, and Explosives (ATF); and Office of Justice Programs (OJP) are discussed below.

Drug Enforcement Administration (DEA). The DEA was created in 1973 to consolidate and coordinate the government's drug control activities by combining the efforts and personnel of four federal drug law enforcement programs. Its legal authority stems primarily from the Controlled Substance Act and other laws directed at control of essential chemicals and precursors. The DEA operates domestically and in foreign countries with the agreement of the government in each country to enforce regulations concerning importation, manufacture, storage, and dispensing of all drugs scheduled under the Controlled Substances Act.

In 2008, DEA employed nearly 11,000 special agents and support staff. Its enforcement programs include asset forfeiture, aviation, computer forensics, demand reduction, diversion control, marijuana eradication, money laundering, and organized crime. Each program was designed to focus on a specific drug threat or facet of the illicit drug trade. Other efforts, such as the Southwest Border Initiative, focused on specific regions of the country identified as primary distribution or manufacturing areas.

In addition to the enforcement efforts described above, the DEA supports intelligence efforts such as the El Paso Intelligence Center (EPIC), a fully coordinated, tactical intelligence center supported by databases and resources from twelve member agencies. EPIC was designed to enable agents to target, track, and interdict drugs, aliens, and weapons moving across U.S. borders.

Federal Bureau of Investigation (FBI). In 1982, FBI resources were significantly expanded and it was given concurrent jurisdiction with the DEA to investigate drug offenses. The FBI concentrates primarily on drug trafficking by organized crime and violent gangs and drug-related financial activities such as international money laundering. Investigations are conducted using electronic surveillance techniques and other law enforcement techniques. In 2007, the FBI had more than 30,000 employees, including more than 12,000 special agents and nearly 18,000 support professionals.

Bureau of Alcohol, Tobacco, Firearms and Explosives (ATF). In 2003, the ATF was transferred from the Department of Treasury to the Department of Justice. In the process the function of ATF shifted from tax and trade functions to an expanded law enforcement focus. The mission subsequently involved both enforcing federal criminal laws and regulating the firearms and explosives industries. ATF is committed to working directly, and through partnerships, to investigate and reduce crime involving firearms and explosives, acts of arson, and illegal trafficking of alcohol and tobacco products. The combined efforts of special agents and industry operations investigators allow ATF to effectively identify, investigate, and recommend for prosecution violators of the federal firearms, explosives, arson, and tobacco and alcohol diversion laws.

As of 2008, ATF was the lead agency in the DOJ Project Safe Neighborhoods, which focuses on reducing gun violence. In addition, ATF worked to prevent terrorism and monitor firearm licensees and provide a variety of resources to other law enforcement agencies, including the National Integrated Ballistic Information Network, gun tracing, national response teams, and national laboratory services.

Office of Justice Programs (OJP). After 1984, OJP developed the capacity to prevent and control crime by generating statistics on law enforcement and crime, supporting research, and funding criminal justice programs. As of 2008, OJP maintained seven bureaus and offices, including the Bureau of Justice Assistance (BJA), the Bureau of Justice Statistics (BJS), and the National Institute of Justice (NIJ). BJA provides technical and financial assistance to state and local governments through formula grants designed to support the enforcement of local and state laws, including drug laws, and to provide resources and intelligence to the law enforcement agencies enforcing these laws. BJS collects, analyzes, and disseminates information on crime, its victims, and its perpetrators. NIJ is the major research and development entity within the DOJ. Its activities include evaluating the effectiveness of programs supported by BJA.

In addition, DEA, FBI, and ATF participate in joint operations run by DOJ, such as the Asset Forfeiture Program, and other agencies, such as the Office of National Drug Control Policy's High Intensity Drug Trafficking Areas Program described below. These efforts are designed to focus on specific drug threats, drug trafficking organizations, or regions of the country.

OFFICE OF NATIONAL DRUG CONTROL POLICY (ONDCP)

The White House Office of National Drug Control Policy (ONDCP) is a part of the Executive Office of the President. It was established by the Anti-Drug Abuse Act of 1988. The principal purpose of ONDCP is to establish policies, priorities, and objectives for U.S. drug control programs. The goals of the program are to reduce illicit drug use, manufacturing, and trafficking; drug-related crime and violence; and drug-related health consequences. ONDCP works with the National Drug Intelligence Center to prepare annual drug threat assessments and reports on U.S. drug

	FY 2007 final	FY 2008 enacted	FY 2009 request
		Budget authority in millions	
Department of Defense	1,329.8	1,177.4	1,060.5
Department of Education	495.0	431.6	218.1
Department of Health and Human Services			
Centers for Medicare & Medicaid Services	—	45.0	265.0
Indian Health Service	148.2	173.2	162.0
National Institute on Drug Abuse	1,000.0	1,000.7	1,001.7
Substance Abuse and Mental Health Services Administration	2,443.2	2,445.8	2,370.6
Total HHS	**3,591.4**	**3,664.8**	**3,799.3**
Department of Homeland Security			
Office of Counternarcotics Enforcement	2.5	2.7	4.0
Customs and Border Protection	1,968.5	2,130.9	2,191.9
Immigration and Customs Enforcement	422.8	412.3	428.9
U.S. Coast Guard	1,080.9	1,004.3	1,071.0
Total DHS	**3,474.8**	**3,550.1**	**3,695.8**
Department of the Interior			
Bureau of Indian Affairs	2.6	6.3	6.3
Total DOI	**2.6**	**6.3**	**6.3**
Department of Justice			
Bureau of Prisons	65.1	67.2	69.2
Drug Enforcement Administration	1,969.1	2,105.3	2,181.0
Interagency Crime and Drug Enforcement	497.9	497.9	531.6
Office of Justice Programs	245.5	222.8	114.2
Total DOJ	**2,777.7**	**2,893.2**	**2,896.0**
ONDCP			
Counterdrug Technology Assessment Center	20.0	1.0	5.0
High Intensity Drug Trafficking Area Program	224.7	230.0	200.0
Other Federal Drug Control Programs	193.0	164.3	189.7
Drug-Free Communities (non-add)	*79.2*	*90.0*	*80.0*
National Youth Anti-Drug Media Campaign (non-add)	*99.0*	*60.0*	*100.0*
Salaries and Expenses	26.8	26.4	26.8
Total ONDCP	**464.4**	**421.7**	**421.5**
Small Business Administration	1.0	1.0	1.0
Department of State			
Bureau of International Narcotics and Law Enforcement Affairs	1,055.7	640.8	1,173.2
United States Agency International Development	239.0	361.4	315.3
Total State	**1,294.7**	**1,002.2**	**1,489.0**
Department of Transportation			
National Highway Traffic Safety Administration	2.9	2.7	2.7
Department of Treasury			
Internal Revenue Service	55.6	57.3	59.2
Department of Veterans Affairs			
Veterans Health Administration	354.1	447.2	465.0
Total	**$13,844.0**	**$13,655.4**	**$14,114.4**

NOTE: Detail may not add due to rounding.
In addition to the resources displayed in the table above, the Administration requests $385.1 million in FY 2008 supplemental funding for counternarcotics support to Mexico and Central America.

Table 1. Drug control funding by agency, FY 2007–FY 2009. (Source: National Drug Control Strategy, 2008 Annual Report. Office of National Drug Control Policy.) ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

control strategy. ONDCP's key drug law enforcement and supply control initiative is the High Intensity Drug Trafficking Areas Program. Other initiatives focus on prevention, treatment, and recovery.

HIGH INTENSITY DRUG TRAFFICKING AREAS (HIDTA) PROGRAM

The purpose of the High Intensity Drug Trafficking Areas (HIDTA) Program is to provide resources to federal, state, and local agencies to

coordinate and carry out activities that address drug trafficking activities in specially designated regions of the United States. The HIDTA Program was first authorized in the Anti-Drug Abuse Act of 1988, the same statute that created the Office of National Drug Control Policy (ONDCP), and it has been reauthorized on three occasions, for example, in the ONDCP Reauthorization Act of 2006. That statute authorized the director of ONDCP to designate an area as a HIDTA only if the following apply:

- the area is a significant center of illegal drug production, manufacturing, importation, or distribution
- state, local, and tribal law enforcement agencies have committed resources to respond to the drug trafficking problem in the area, thereby indicating a determination to respond aggressively to the problem
- drug-related activities in the area are having a significant harmful impact in the area and in other areas of the country
- a significant increase in allocation of federal resources is necessary to respond adequately to drug-related activities in the area.

In 1990, the director of ONDCP designated the first five HIDTAs in Los Angeles, Houston, Miami, New York, and along the entire length of the southwest U.S.-Mexico border. These five regions were considered to be gateways for the entry of illegal drugs into the United States. As the advantages of the HIDTA Program became apparent, the program was expanded to include other areas in which drug trafficking problems met the statutory requirements. As of 2008, there were twenty-eight HIDTAs located in forty-three states plus Puerto Rico, the U.S. Virgin Islands, and the District of Columbia. These HIDTAs include more than 13 percent of all counties in the United States and approximately 60 percent of the U.S. population. In 2006, more than 20,000 federal, state, and local law enforcement officers and other staff participated in the HIDTA Program.

The mission of the HIDTA Program is to disrupt the market for illegal drugs in the United States by assisting federal, state, and local law enforcement HIDTA participants in dismantling and disrupting drug trafficking organizations. Simply put, the mission is to take traffickers and drugs off the streets of the United States. To accomplish this mission, the HIDTA Program provides an infrastructure and coordinated umbrella for participating law enforcement agencies to enable it to combine and leverage resources and capabilities and expand the scope of its investigations.

To monitor the effectiveness and efficiency of this approach, the HIDTA directors developed the Performance Management Process (PMP). The PMP involves six key phases that are completed annually: identifying threats and needs, setting performance targets and implementing a strategy for achieving them, identifying a measurement protocol, budgeting for results, monitoring and managing results, and reporting on the outcomes. In 2006, the operations of 2,522 drug trafficking organizations and money laundering organizations were either completely dismantled or disrupted to the point where their ability to operate was severely diminished. More than $16 billion worth of illegal drugs, more than $834 million in illegally gained assets, and 1,522 clandestine labs capable of producing a minimum of $12 million worth of methamphetamine per year were seized. For every dollar invested in HIDTA enforcement and intelligence initiatives, the HIDTA Program took $92 in illegal drugs off the streets and seized nearly $5 in cash and other assets.

DEPARTMENT OF HOMELAND SECURITY

The Department of Homeland Security (DHS) was established as a part of the Homeland Security Act of 2002 to provide the unifying core for the vast national network of organizations and institutions involved in efforts to secure the United States. As of 2008, the four entities housed in DHS that touch on drug law enforcement and supply control were the U.S. Citizenship and Immigration Services (USCIS), Bureau of Customs and Border Protection (BCBP), Bureau of Immigration and Custom's Enforcement (ICE), and the Office of Immigration Statistics (OIS). Each of these entities is actively involved in protecting U.S. borders and disrupting smuggling activities. ICE was established in March 2003 as the largest investigative arm of the DHS. It works with U.S. and foreign authorities to locate and apprehend dangerous individuals running or involved in drug trafficking organizations. Through

Operation Community Shield, ICE agents partner with federal, state, and local law enforcement to target violent transnational street gangs through the use of ICE's broad law enforcement powers, including the unique and powerful authority to remove (deport) criminal aliens, including illegal aliens and legal permanent resident aliens. ICE agents also participated in HIDTA initiative investigations of drug trafficking organizations across the country.

OTHER FEDERAL DEPARTMENTS

Other federal departments involved in drug law enforcement and supply control include the Department of Transportation, the Department of Defense, the U.S. Postal Service, and the Department of State. The Federal Aviation Administration and U.S. Coast Guard in the Department of Transportation and the Department of Defense use radar systems and other technology to detect and interdict drug smuggling by air and water. The U.S. Postal Service investigates smuggling efforts using mail services. The Department of State establishes international antidrug policies and coordinates drug control efforts with foreign governments.

See also **Controlled Substances Act of 1970; Crime and Drugs; Drug Interdiction; International Drug Supply Systems; Terrorism and Drugs.**

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AGENCIES SUPPORTING SUBSTANCE ABUSE PREVENTION AND TREATMENT

Within the U.S. Department of Health and Human Services (DHHS), originally established in 1953 as the Department of Health, Education, and Welfare (DHEW), a number of Public Health Service (PHS) agencies have been involved in reducing drug abuse. From 1974 to 1992 many demand-reduction activities were related to increasing, through research, the scientific foundations for a better understanding of how drugs of abuse interact with individuals, so as to prevent drug abuse and effectively treat those who do abuse drugs. Included among these agencies are the National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), both components of the National Institutes of Health (NIH), as well as the Center for Substance Abuse Prevention (CSAP) and the Center for Substance Abuse Treatment (CSAT), components of the Substance Abuse and Mental Health Services Administration (SAMHSA). In addition, the Health Resources and Services Administration (HRSA) and the National Institute of Child Health and Human Development (NICHD), another NIH component, play a role in the department's anti-drug abuse mission.

From its creation in 1974 by statute, the National Institute on Drug Abuse has conducted research on drugs of abuse and their effects on individuals. In its early days, NIDA supported prevention and treatment programs and conducted clinical training programs for professional healthcare workers (particularly in schools of medicine, nursing, and social work), counselors and other paraprofessionals. With the advent of the Alcohol and Drug Abuse and Mental Health Services block grant, enacted into statute in 1981, the direct provision of treatment and prevention services became a state responsibility. Enactment of the block grant that is currently administered within SAMHSA refocused the NIDA role on the generation of knowledge through scientific research so that more could be learned about strategies and programs to prevent and treat drug abuse.

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) conducts research on alcohol abuse and alcoholism. Because a comprehensive approach to prevention and treatment of drug abuse requires attention to alcohol as well as to

illicit drugs, and because individuals who abuse illicit drugs often abuse alcohol as well, the research programs of NIDA and NIAAA are symbiotic. Furthermore, the genetic, environmental, and social influences important to the initiation of drug and alcohol use are similar, and research in one area suggests researchable hypotheses in the other.

The Center for Substance Abuse Prevention (CSAP), established in 1986 as the Office for Substance Abuse Prevention (OSAP), has led national efforts to prevent alcohol and other drug use, with a special emphasis on youth and families at particularly high risk for drug abuse. Youth considered to be at high risk include school dropouts, economically disadvantaged youth, or children of parents who abuse drugs or alcohol or who are at high risk of becoming drug or alcohol abusers. CSAP administers a variety of programs, including prevention demonstration grants targeting youth at high risk and pregnant and postpartum women and their infants.

The Center for Substance Abuse Treatment (CSAT), formerly the Office of Treatment Improvement (OTI), was established administratively in 1990 to improve treatment services and expand the capacity for delivering treatment services. CSAT administers the State Substance Abuse Prevention and Treatment block grant and undertakes knowledge development, education, and communications initiatives that promote best practices in substance use/abuse treatment and intervention. The CSAT Targeted Capacity Expansion Program—and its specialized program focused on HIV/AIDS services—help communities respond rapidly to emerging local drug use trends.

Drug and alcohol abuse are complex behaviors that often result in a multitude of adverse consequences. Thus, to understand them necessitates multifaceted, often crosscutting, areas of research. Because many individuals who suffer from alcohol or drug abuse also suffer from mental illness (called *co-occurring disorders*), NIAAA and NIDA, as well as the National Institute of Mental Health (NIMH) of the NIH, are engaged in initiatives to learn more about individuals who have co-occurring disorders.

Acquired immunodeficiency syndrome (AIDS) has become a chronic health concern among intravenous drug users, and an increased risk of human immunodeficiency virus (HIV) infection in those who share drug paraphernalia with other drug users has been clearly demonstrated. Accordingly, NIDA collaborates with the Centers for Disease Control (CDC) on AIDS prevention programs and with the National Institute of Allergy and Infectious Diseases (NIAID) to provide HIV therapeutics to intravenous drug abusers with HIV.

The study of maternal and fetal effects of drug abuse is another high-priority focus within the department. Research and demonstration programs have been undertaken by NIDA and CSAP, and the NICHD is also conducting studies in this area.

Recent research has shown that the most effective treatment for drug abusers is a comprehensive array of services that address not only their drug-abuse problems but also other health problems and their potential need for education and vocational rehabilitation as well as a host of ancillary services. Accordingly, NIDA, the centers within SAMHSA, and HRSA are exploring the effectiveness of providing a comprehensive range of services in drug-abuse and primary-care settings.

In addition to the DHHS, many other agencies are involved in prevention and treatment efforts. For example, the Food and Drug Administration (FDA) plays a determining role in deciding when new pharmacological treatment agents can be marketed for clinical use, and it is one of the key agencies setting policies and standards for the use of opioid drugs in the treatment of opioid dependence. Both the Department of Education and the Department of Justice (through the Drug Enforcement Administration [DEA]) have significant programs aimed at prevention; the Department of Veterans Affairs and the Department of Defense (U.S. military) have also made major commitments to treatment.

See also **Prevention, Education and; Substance Abuse and AIDS.**

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AGENCIES SUPPORTING SUBSTANCE ABUSE RESEARCH

In the United States, federal support of drug-abuse research began in the 1920s with the work of Lawrence Kolb. It became more formalized with the establishment of the Addiction Research Center in 1935. By 1944 a small research unit was formed with only 15 employees in a U.S. Public Health Service Hospital in Lexington, Kentucky. The Addiction Research Center was designed for federal prisoners who were narcotics addicts. This research group became part of the National Institute of Mental Health (NIMH) in 1948, the year the institute was established. In 1979 the Addiction Research Center moved to Baltimore, Maryland, and became the in-house (intramural) research program of the National Institute on Drug Abuse (NIDA), which had been established by Congress in 1974.

For fiscal year 2009 (FY 2009), NIDA's budget was estimated at more than one billion dollars. The research thus funded included studies in practically every basic and clinical science, both biomedical and social. The National Institute on Alcohol Abuse and Alcoholism (NIAAA), established in 1970, conducts parallel efforts in the area of alcohol-abuse research. In FY 2009, NIAAA funded more than 200 grants, with a budget of nearly $437,000,000.

Both NIDA and NIAAA became part of the National Institutes of Health (NIH) in October 1992. They had previously been part of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), which included both research and services components. By separating these two components, Congress indicated its intention to give proper emphasis to both. Treatment and prevention services for alcohol and drug abuse are under the direction of the Substance Abuse and Mental Health Services Administration (SAMHSA).

NIDA and NIAAA are the two largest federal research institutes dedicated to drug abuse and alcohol research, but many other agencies have a stake in these areas. They include other institutes in the NIH; for example, the Eunice Kennedy Shriver National Institute of Child Health and Human Development focuses a significant portion of its research on the effects of drugs and alcohol on fetal development and on the consequences for the neonate of exposure to drugs and alcohol during pregnancy. The NIMH conducts research on the high coincidence of mental illness and substance-

abuse disorders. Some of the other institutes have similarly targeted interests as, for example, the National Cancer Institute, which played an important role in support of research on tobacco dependence and the adverse health effects of tobacco. The Centers for Disease Control (CDC) use their epidemiological expertise to resolve certain questions about the nature and extent of the abuse of drugs and alcohol.

Beyond the Public Health Service and the Department of Health and Human Services, many other federal agencies and departments are concerned with and conduct research on the social problems caused by drug and alcohol abuse: the Departments of Education, Labor, Transportation, Treasury, Justice, State, Veterans Affairs, and even Defense—each has a stake in drug-abuse research. The Department of Education is concerned primarily with drug and alcohol prevention; the Departments of Labor and Transportation, with workplace performance impaired by drugs and alcohol.

The Department of Veterans Affairs has played an important role in both basic and clinical research. Some of the most important work on the treatment of opioid dependence as well as on alcoholism and the toxic effects of alcohol has been conducted by researchers based at Veterans Administration (VA) hospitals and funded in part by the Department of Veterans Affairs. Other federal agencies have a regulatory role in drug-abuse research. Many of the drugs that are studied in animals and volunteer human subjects are included under the Controlled Substances Act of 1970. In order to obtain and store the drugs, researchers must be properly registered with the Drug Enforcement Administration (DEA). The DEA is also responsible for ensuring that the drugs are properly stored and that researchers keep records of their use. In addition, researchers who are interested in studying any drug not yet approved for clinical use or in studying an approved drug for a new use (such as using the analgesic drug buprenorphine to combat opiate addiction) must obtain an Investigational New Drug (IND) authorization from the Food and Drug Administration (FDA). Further, when a new agent seems promising, a sponsor (usually a pharmaceutical company) must submit the data supporting its safety and effectiveness to the FDA before it can be approved for marketing and general use.

Both the Department of Justice and the Department of the Treasury are concerned with law enforcement issues surrounding drug and alcohol use, and they have funded research on detection of clandestine laboratories and the nature of club and designer drugs. In 2008 the Department of Homeland Security spent $4 million on counternarcotics enforcement, and the Department of the Treasury, via the IRS, targeted $59.2 million toward drug control efforts.

The Department of State and the Department of Defense are also involved in matters relating to international narcotics control. The 2009 National Drug Control Strategy earmarked one billion dollars of the Department of Defense's funding for drug control spending. Department of Justice's FY 2009 DEA spending was estimated at around $2.2 billion.

Congress in 1988 mandated the Office of National Drug Control Policy (ONDCP) to coordinate the federal antidrug-abuse effort. The Office of the President develops the annual National Drug Control Strategy with its accompanying budget summary. It contains three areas of emphasis: (1) stopping use before it starts; (2) intervening and healing America's drug users; and (3) disrupting the market. For FY 2009, the drug budget totaled $14.1 billion, an increase of 3.4 percent or $459 million from the previous budget. The Administration also requested $385.1 million for counternarcotics support to Central America and Mexico under the Merida Initiative. Fostering improved security cooperation between the United States, Mexico, and Central America is the focus of the Merida Initiative, a multi-year $1.4 billion program aimed at decreasing cross-national crime. In FY 2008, ONDCP requested a budget supplement of $385.1 million to launch the program. The supplemental request for Merida in FY 2009 was $432.2 million. All of these policy-related organizations rely on facts based on the biomedical, epidemiological, and behavioral research funded by NIDA, NIAAA, and NIMH.

See also **Prevention, Education and; Wikler's Conditioning Theory of Drug Addiction.**

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U.S. GOVERNMENT AGENCIES

This entry includes the following essays:

BUREAU OF NARCOTICS AND DANGEROUS DRUGS (BNDD)

Presidential Reorganization Plan No. 1 of 1968 created the Bureau of Narcotics and Dangerous Drugs (BNDD) in the U.S. Department of Justice. The new agency combined the drug law enforcement functions of two predecessor organizations—the Federal Bureau of Narcotics (FBN) in the Department of the Treasury and the Bureau of Drug Abuse Control in the Food and Drug Administration, Department of Health and Human Services. Long-standing conflicts between two Department of the Treasury agencies that shared drug-enforcement responsibilities—the Federal Bureau of Narcotics and the Bureau of Customs—led to the decision to move the FBN functions into a new agency (BNDD) in a different cabinet department (Justice).

MISSION AND EXPERIENCE

BNDD's role was to suppress illicit narcotics trafficking and to control the diversion of legally manufactured drugs. BNDD was responsible for working with foreign governments to halt international drug traffic, immobilizing domestic illegal drug-distribution networks, providing a wide range of technical assistance and training to state and local officers, and preparing drug cases for prosecution.

BNDD emphasized investigations of high-level drug trafficking to identify and target major

national and international violators. Director John E. Ingersoll described the success of BNDD as being "able to apprehend scores of illicit drug traffickers who were previously immune to the feeble efforts which law enforcement was formerly able to mount." In 1968 and 1969, BNDD contributed to major international success in stopping heroin traffic originating in Turkey.

The Bureau of Customs continued interdiction of drug smuggling at the borders and ports of entry. Customs special agents investigated drug cases based on seizures made by Customs inspectors and on antismuggling intelligence. Conflict between BNDD and Customs continued, with allegations of lack of cooperation and failure to share intelligence with each other.

The White House and Office of Management and Budget (OMB) tried to resolve the conflict and, in early 1970, President Richard M. Nixon directed BNDD and Customs to work out a set of operating guidelines. After considerable interagency discussion, formal guidelines were prepared to give to BNDD full jurisdiction over drug-enforcement operations both within the United States and overseas. Customs was to be limited to border operations. The president approved the guidelines, but the conflicts continued. Neither Congress nor the White House was satisfied. Senator Abraham Ribicoff described the detailed guidelines as "more reminiscent of a cease-fire agreement between combatants than a working agreement between supposedly cooperative agencies."

ADDITIONAL DRUG ENFORCEMENT COMPLICATIONS

The "war against drugs" continued to expand. In 1972, President Nixon established two new drug agencies in the Department of Justice—the Office of Drug Abuse Law Enforcement (ODALE) and the Office of National Narcotics Intelligence (ONNI). ODALE's operational involvement with state and local law enforcement against local drug dealers was intended to complement BNDD's focus on high level traffickers. ODALE, however, depended on existing federal agencies for agents and attorneys, and BNDD was required to lend over 200 narcotics agents to ODALE. The additional antidrug agencies, combined with sensational reporting of conflicts between special agents from BNDD and Customs, added to the public perception of fragmentation and disorder in federal drug law enforcement.

In early 1973, another presidential reorganization plan was designed to eliminate the overlap and duplication of effort in drug enforcement. A factual assessment of the BNDD/Customs situation, provided to the Congress by the chief of OMB's Federal Drug Management Division, Walter C. Minnick, reported "Having attempted formal guidelines, informal cooperation and specific Cabinet-level mediation, all without success, the President concluded in March of 1972 that merging the drug investigative and intelligence responsibilities of Customs and BNDD into a single new agency was the only way to put a permanent end to the problem." Under Reorganization Plan No. 2 of 1973, BNDD, ODALE, and ONNI were eliminated; their functions and resources, along with 500 Customs special agents (those previously involved in drug investigations), were consolidated in the new Drug Enforcement Administration (DEA) in the Department of Justice.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy.**

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CENTER FOR SUBSTANCE ABUSE PREVENTION (CSAP)

The Center for Substance Abuse Prevention (CSAP) was originally established as the Office for Substance Abuse Prevention (OSAP). It was created by the Anti-Drug Abuse Act of 1986 for the prevention of alcohol and other drug problems among U.S. citizens, with special emphasis on youth and families living in high-risk environments. From 1986 to 1992, OSAP operated as a unit of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), one of the eight Public Health Service agencies within the U.S. Department of Health and Human Services. In 1992, Public Law 102–321 reorganized ADAMHA and renamed it the Substance Abuse and Mental Health Services Administration (SAMHSA); it also created CSAP to replace OSAP.

The stated mission of CSAP is to bring effective substance abuse prevention to every community. On the federal level, CSAP is tasked with leading the nation's efforts to eliminate alcohol, tobacco, and drug use problems. To improve the health and quality of life for people across the nation, CSAP employs a community-based, structured prevention approach through its Strategic Planning Framework (SPF). The SPF is designed to provide education, tools, and techniques for the creation of a broad-based prevention framework that can be easily employed and replicated by the states, regions, and local communities. The goal of the SPF is to target youth: to provide education about risk reduction (offering healthier alternatives to risk-taking behaviors) and to build on existing strengths, skills, and resiliency as a means of preventing youth from making negative choices. By fostering greater strengths in young people, the SPF intends to promote healthier choices throughout life.

The primary goal of CSAP is to promote choosing not to use illicit drugs and refraining from illegal or high-risk use of alcohol or other legal drugs. High-risk alcohol use includes drinking and driving, drinking while pregnant, drinking while recovering from alcoholism and/or when using certain medications, having more than two drinks a day for men and more than one for women, and drinking to intoxication.

These are the principles that guide the prevention work of CSAP:

1. The earlier prevention is started in a person's life, the more likely it is to succeed.
2. Prevention programs should be knowledge-based and should incorporate state-of-the-art findings and practices drawn from scientific research and field expertise.
3. Prevention programs should be comprehensive and take a strengths-based approach.
4. Programs should include both process and outcome evaluations.
5. The most successful programs are those initiated and conducted at the community level.

To utilize these principles and achieve its goals, CSAP performs the following functions:

1. Carries out demonstration projects targeting specific groups and individuals in high-risk environments.
2. Assists communities in developing long-term, comprehensive alcohol and other drug use prevention and early intervention programs.
3. Operates a national clearinghouse for publications on prevention and treatment and other materials and services.
4. Supports the National Training System, which develops new drug use prevention materials and delivers training.
5. Supports field development.
6. Utilizes numerous assessment tools: the prevention platform, state prevention profiles, national outcome measures, state juvenile justice profiles, and the Helping America's Youth Program Tool Database.
7. Conducts an evaluation strategy consisting of individual grantee evaluations, contractual program-wide evaluations, and the National Evaluation Project.
8. Provides technical assistance for capacity building and promotes collaborations to help states, communities, and organizations develop and implement communications, drug use prevention, and early intervention efforts.
9. Develops and implements public information and educational media campaigns and other

special-outreach and knowledge-transfer prevention programs.

10. Maintains a national drug use prevention database to provide information on substance-abuse prevention programs.
11. Provides technical assistance and materials to small businesses for the development of employee-assistance programs.
12. Operates the SAMHSA's Prevention Platform, which is targeted to ensure that local community prevention programs achieve successful outcomes. The program is Web-based and user-friendly.

To promote interagency cooperation and facilitate jointly sponsored prevention activities, CSAP's staff meets routinely with various federal organizations, including the departments of Defense, Justice, Education, Transportation, Labor, and Housing and Urban Development; the Bureau of Indian Affairs; and others.

CSAP also develops partnerships with the research community, parent groups, foundations, policymakers, health-care practitioners, faith-based community programs, state and community leaders, educators, law enforcement officials, and others to enhance opportunities for comprehensive approaches to prevention and early intervention.

See also **Parent Movement, The; Prevention, Education and.**

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CENTER FOR SUBSTANCE ABUSE TREATMENT (CSAT)

The Center for Substance Abuse Treatment (CSAT) was established in January 1990 as the Office for Treatment Improvement (OTI) of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) within the Department of Health and Human Services (DHHS). Dr. Beny J. Primm, a physician who had spent more than 20 years developing a major treatment program in New York City, was appointed as its first director. Following the reorganization of ADAMHA in 1992, the agency was renamed and is now part of the Substance Abuse and Mental Health Services Administration (SAMHSA), which replaced ADAMHA.

The congressional mandate of CSAT is to expand the availability of effective treatment and recovery services for people with drug and alcohol problems. One of its goals is to ensure that new treatment technology is absorbed by the addiction-treatment infrastructure, the system of state and local government agencies and public and private treatment programs providing addiction-treatment services. In carrying out this responsibility, CSAT collaborates with states, communities, and treatment providers to upgrade the quality and effectiveness of treatment and enhance coordination among drug-treatment providers; human services, educational, and vocational services; the criminal justice system; and a variety of related services. CSAT provides financial and technical assistance to targeted geographic areas and patient populations, with an emphasis on assistance to minority racial and ethnic groups, youth and adolescents, homeless and displaced persons, women of childbearing age, and people living in frontier or in rural areas.

CSAT also collaborates with other government agencies, such as the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute of Mental Health (NIMH), and the Center for Substance Abuse Prevention (CSAP), as well as state and local governments, to promote the utilization of effective means of treatment and develop treatment standards. In addition, CSAT has interagency agreements with the Department of Labor and the Department of Education that are designed to improve the coordination of health and human services, education, and vocational training. CSAT also promotes the mainstreaming of alcohol, drug abuse, and mental health treatment into the primary health-care system, and is responsible for administering the Substance Abuse

Prevention and Treatment (SAPT) Block Grant program, which provides federal support to state substance-abuse prevention and treatment programs (the total appropriation for 2007 was $1,758,591,000).

Research has generated a vast body of knowledge regarding the nature of chemical dependency and about what works in the treatment of addiction and addiction-related health and mental health disorders. From this research, three key observations formed the basis for CSAT's initial treatment philosophy. First, addiction is a complex phenomenon and cannot be treated in isolation from addressing the primary health, mental health, or socioeconomic deficits of addicted persons. Second, addiction is frequently a chronic, relapsing disorder, and the gains made during treatment are often lost following a person's return to the community. CSAT therefore tried to foster programs that provided those treated for chemical dependency with a series of interventions along a sustained continuum. These two observations constituted the basis for CSAT's Comprehensive Treatment Model, which was a central principle in all of its demonstration grant programs and technical-assistance initiatives.

During its first few years of existence, CSAT targeted resources to the people it perceived as most adversely affected by extreme socioeconomic problems and at highest risk for addiction because of exposure to crime, abuse, poverty, and homelessness, or because of a lack of access to primary health and mental health care, social services, and vocational training and education. For this reason, the early Comprehensive Treatment Model demonstration grants fostered a wide array of primary interventions geared to addressing each patient's health and human service needs, coupled with a readily accessible, intensive aftercare component.

At the core of CSAT's overall approach is the conviction that treatment works, the third key observation. Treatment has proved effective in reducing the use of illicit drugs and alcohol, improving rates of employment, reducing rates of human immunodeficiency virus (HIV) seroconversion, reducing criminal activity, and reducing overall patient morbidity.

In addition to the SAPT Block Grant, CSAT awarded grants for a variety of demonstration and service programs. Access to Recovery (ATR) is a three-year SAMHSA-funded grant. ATR provides consumers with vouchers that can be used to purchase clinical treatment and recovery support services for substance abuse disorders. ATR is designed to expand the capacity of funded service providers, thereby increasing consumer choice. Partners for Recovery (PFR) provides support and technical assistance to providers of substance abuse prevention and treatment services. The Knowledge Application Program (KAP) produces written and electronic media for substance abuse consumers and treatment providers. The Treatment Improvement Protocol (TIP) series and Technical Assistance Publications (TAPs), under the auspices of KAP, create and distribute consumer-targeted literature as well and technical and training manuals and guides for providers.

The National Center on Substance Abuse and Child Welfare (NCSACW) seeks to improve outcomes for families involved in the child welfare and judicial systems by partnering with local, state, and tribal judiciaries. Medication-Assisted Treatment (MAT) augments traditional behavioral substance abuse treatment models with the judicious use of medications in order to facilitate recovery. The Recovery Community Services Program (RCSP) utilizes a peer-to-peer recovery support model as a means of aiding individuals in recovering (and maintaining recovery) from substance abuse disorders. The Screening, Brief Intervention, and Referral to Treatment (SBIRT) program is a comprehensive, integrated, multidisciplinary public health model for delivery of early intervention and treatment services for persons with substance abuse disorders (SUDs), coupled with a prevention program aimed at reducing the incidence of SUDs.

Since the mid-1990s, CSAT's demonstration grant program has broadened to encompass not only the improvement of services for those populations in greatest need, but also to develop a knowledge base about the effectiveness of treatment for different subgroups of the drug-using population.

See also **Treatment: An Overview.**

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NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) is the principal federal agency for research on the causes, consequences, treatment, and prevention of alcohol-related problems. NIAAA supports studies in both biological and behavioral research, research training and health professions development programs, and research on alcohol-related public policies. The FY2008 budget for the NIAAA was in excess of $436.5 million.

ORGANIZATION

NIAAA is one of 27 research institutes and centers of the prestigious National Institutes of Health (NIH), a component of the U.S. Department of Health and Human Services. The mission of the NIAAA is to lead the nation in the efforts to reduce alcohol-related problems. This is accomplished by managing a large-scale scientific research program encompassing genetics, neuroscience, epidemiology, health risk management, treatment, and prevention:

- By collaboration and coordination with other private, state, and federal research, treatment and prevention programs;
- By working in collaboration with alcohol-related facilities, organizations, programs, and agencies—both within the United States and abroad;
- By communication of the research results and outcome findings to the general public, the scientific and research communities, and to policymakers and legislators

The goals of the work of the NIAAA are threefold: (1) to increase the understanding of normal and abnormal behavior and biology in the context of alcohol use; (2) to facilitate effective diagnosis, treatment, prevention, and early intervention of alcohol abuse and dependence; and (3) to improve continual health care quality.

Under the auspices of the Office of the Director, there are three principal offices and five divisions that manage and coordinate NIAAA activities.

- Office of Extramural Activities
- Office of Science Policy and Communications
- Office of Resource Management and the Division of Intramural Clinical and Biological Research
  - ——Division of Epidemiology and Prevention Research
  - ——Division of Metabolism and Health Effects
  - ——Division of Neuroscience and Behavior
  - ——Division of Treatment and Recovery Research

NIAAA supports research principally through extramural grants awarded to scientists at leading U.S. research institutions and through research conducted by NIAAA's own intramural staff scientists. Findings from these research areas are made available and accessible through a wide variety of research dissemination activities.

INTRAMURAL RESEARCH

Intramural research is carried out under the auspices of the Division of Intramural Clinical and Biological Research. Scientists in the NIAAA Intramural Research Program (IRP) focus on research opportunities that allow intensive, long-term commitment as well as the flexibility to adjust research priorities in response to new findings. Because clinical and laboratory studies occur side by side, new

findings from basic research may be readily transferred for appropriate testing and application, and clinical hypotheses may be in turn posited to lab scientists. Areas of study include (a) identification and assessment of genetic and environmental risk factors for the development of alcoholism; (b) effects of alcohol on the central nervous system including how alcohol modifies brain activity and behavior; (c) metabolic and biochemical effects of alcohol on various organs and systems of the body; (d) noninvasive imaging of the brain structure and activity related to alcohol use; (e) development of animal models of alcoholism; and (f) diagnosis, prevention, and treatment of alcoholism and associated disorders. NIAAA uses a combination of clinical and basic research facilities that enable a coordinated interaction between basic research findings and clinical applications in pursuit of these goals. A 12-bed inpatient unit and a large outpatient program are located in the NIH Clinical Center in Bethesda, Maryland.

The primary goal for the intramural research program is to clearly define and understand the means by which alcohol intoxication, dependence and subsequent physiological damage to vital organs occurs, and to develop effective behavioral and biological intervention and prevention strategies. Some of the current areas of focus for intramural research involve (a) genetic studies designed to identify and describe the genes involved in alcohol use disorders by increasing genetic vulnerability to alcohol abuse and dependence; (b) determination of the foundations of alcohol-related liver disease; (c) epidemiological studies on prevalence of alcohol-related use, abuse, and dependence; (d) research on the neurophysiology and behavioral mechanisms stimulating the desire to consume alcohol; (e) identification of environmental risk factors acting as a precursor to alcohol abuse or dependence; (f) central nervous system effects of alcohol use; (g) brain imaging of the effects of alcohol use; (h) animal models predictive of human alcohol use disorders; and (i) research on the neurobiology of alcohol dependence, aimed at the creation of improved prevention and early intervention strategies.

EXTRAMURAL RESEARCH

Division of Epidemiology and Prevention Research. External research is supported by four extramural divisions that provide grant dollars and support to cutting-edge research facilities across the United States. The Division of Epidemiology and Prevention Research (DEPR) focuses on the reduction of alcohol-related disorders, mortality, and morbidity through the use of epidemiological and prevention studies—funding and supporting research and scholarly publications, training, and professional and scientific workforce development, involvement in alcohol use surveillance, and communication of research results to the general public. This research program provides the foundation for monitoring the health of the population, developing and evaluating prevention and treatment services for alcohol problems, and establishing alcohol-related social policies. NIAAA-supported epidemiology research examines the context, volume, and specific drinking patterns that lead to particular alcohol-related problems. It also studies the impact of age, gender, race or ethnicity, and other sociodemographic factors as well as genetic, environmental, and other factors that influence injury or disease occurrence.

The two overarching areas of interest for DEPR are epidemiology and prevention. The epidemiology research arm seeks to understand the (a) etiology and progression of alcohol use disorders (AUDs); (b) co-occurrence of AUDs and disorders of physical or mental health; (c) AUDs and behavioral outcomes or consequences such as motor vehicle accidents, negative impact on job performance or stability, decreased academic performance, sexual risk-taking, interpersonal violence, and illness or death; (d) biopsychosocial, socioeconomic, and social-cultural impacts of drinking behaviors; and (e) prevention and early intervention with AUDs; and methodological considerations.

The prevention section conducts research on the efficiency and effectiveness of screening, brief intervention and referral to treatment protocols (SBIRT grants) including comprehensive community prevention programs, total community approach programs, anti-drinking and driving programs, as well as on the impact of the media, alcohol promotion and marketing efforts, and public policy on alcohol-related behaviors.

Division of Metabolism and Health Effects. Chronic consumption of large amounts of alcohol has profound physiological impacts over time.

AUDs during pregnancy can result in one of the fetal alcohol spectrum disorders (FASDs). Across a life span, chronic alcohol use can lead to liver diseases, pancreatitis, cardiomyopathy, and impaired immune and metabolic system functioning. Co-occurring disorders associated with AUDs are type 2 diabetes, hepatitis C, obesity, osteoporosis, degenerative neurological syndromes or dementias, and several types of cancer. The research supported by the Division of Metabolism and Health Effects (DMHE) examines the genetics, metabolism, and immunology contributing to and resulting from AUDs that both cause and advance the above listed disorders. A central goal of DMHE research is to uncover mechanisms for developing medications targeted at treatment and prevention of AUDs. Genetic research is aimed at creation of mechanisms for repair of tissue and organ damage caused by chronic AUDs; both pharmaceutical, such as the use of medications; and physiological, such as stem cell transplants, metabolic manipulations, or gene targeting. In addition to studying the negative effects of alcohol use, DMHE supports research on the potential positive impacts of alcohol consumption on diabetes, some inflammatory processes, and cardiovascular disease.

Division of Neuroscience and Behavior. Many of the behaviors associated with alcohol use problems are the result of alcohol's effects in the brain. NIAAA research is designed to learn how these effects influence the development of alcohol abuse and alcoholism. Molecular biology and genetic techniques, including the use of transgenic animals, are becoming an integral part of this research. In addition noninvasive, functional imaging techniques are used in animal and human studies to identify neural circuits influenced by alcohol. The Division of Neuroscience and Behavior is particularly focused on research concerned with alcohol use during pregnancy resulting in the development of a fetal alcohol spectrum disorder and the long-term effects of alcohol use on the rapidly developing adolescent brain.

Division of Treatment and Recovery Research. The Division of Treatment and Recovery Research studies the progression of alcohol use from heavy drinking through the spectrum of AUDs as well as factors that influence positive changes in alcohol use behavior, whether they are such natural consequences associated with drinking as compromised physical health, job or academic failure, motor vehicle accidents; or within such self- or mutual-help groups as twelve-step programs or community treatment centers; or in professional settings such as hospitals or rehabilitation facilities. There is also ongoing research focused on the treatment of AUDs from a disease prevention and medical management model. Some of this work is aimed at developing medications that decrease the craving for alcohol and thereby decrease recidivism during recovery efforts.

NIAAA continues to emphasize research to improving treatment of alcohol abuse and alcoholism and supports a range of treatment or clinical studies including clinical trials of treatment therapies, patient-treatment matching studies, and behavioral or pharmacological treatment approaches. Prevention research is also aimed at developing effective measures to reduce alcohol-related problems These include the study of alcohol-related intentional and unintentional injury, alcohol-related violence, alcohol in the workplace, drinking and driving deterrence, and the relationship between alcohol availability and alcohol-related problems. New methodologies permit prevention researchers to target high-risk neighborhoods within larger cities.

Cross-Institute and Transdisciplinary Programs. There are several multi-disciplinary programs supported by NIAAA. One of the pivotal activities involves a study of the ways in which alcohol use during pregnancy affects the developing fetus, potentially leading to one of the fetal alcohol spectrum disorders. The Interagency Coordinating Committee on Fetal Alcohol Syndrome (ICCFAS), created in response to an Institute of Medicine report in 1996, is chaired by the NIAAA. The Collaborative Institute on Fetal Alcohol Spectrum Disorders (CIFASD), launched by NIAAA in 2003, is a cooperative agreement program aimed at refining both diagnostic accuracy and developing improved treatment protocols across the entire FASD spectrum. CIFASD research occurs internationally as well as within multidisciplinary sites across the United States.

The NIAAA partnered with the National Institute on Child Health and Human Development in

2003 to create the longitudinal Prenatal Alcohol in Sudden Infant Death Syndrome (SIDS), and Stillbirth (PASS) Network, whose mission is to discern the causes of SIDS and stillbirth and to ascertain the role played by prenatal alcohol use in both syndromes. Twelve thousand pregnant women from South Africa and the Northern Plains and their babies will be studied until the children complete one year of life, in an effort to discern interactions between alcohol use and specific maternal and fetal factors.

Binge drinking, alcohol abuse, and alcoholism are global problems and the NIAAA is involved in a variety of collaborative and cooperative international research programs in these areas. Transdisciplinary programs involve Intramural and Extramural Research Emphasis and Resource Development Teams. The major areas of current interest for the transdisciplinary teams are the genetic and environmental etiology of risk, mechanisms of alcohol action and injury, mechanisms of behavior change, medications development, and research on the causes, consequences, and prevention of underage drinking, particularly adolescent binge drinking.

RESEARCH RESULTS DISSEMINATION

NIAAA shares relevant findings from alcohol research with health care practitioners, policymakers and others involved in managing alcohol-related programs, and the general public through publications in scientific and clinical journals, general and specialized brochures, pamphlets, manuals, clinical bulletins, and several online database services supported by the institute and the NIH:

- Alcohol and Alcohol Problems Science Database. http://etoh.niaaa.nih.gov/
- Alcohol Policy Information System. http://alcoholpolicy.niaaa.nih.gov/
- NESARC: National Epidemiologic Survey on Alcohol and Related Conditions. http://www.nesarc.niaaa.nih.gov/
- NIAAA Data and Statistical Tables. http://www.niaaa.nih.gov/Resources/DatabaseResources/QuickFacts/
- National Library of Medicine: MEDLINE. http://www.nlm.nih.gov/databases/index.html

See also **Accidents and Injuries from Alcohol; Alcohol: An Overview; Epidemiology of Alcohol Use Disorders; Fetal Alcohol Syndrome; Models of Alcoholism and Drug Abuse; National Council on Alcoholism and Drug Dependence (NCADD); Prevention; Prohibition of Alcohol; Temperance Movement; Treatment: An Overview of Alcohol Abuse/Dependence.**

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NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

As of 2008 the National Institute on Drug Abuse was a premier research institute supporting research on the health aspects of drug abuse and addiction. The vast NIDA portfolio supports research on all drugs of abuse from opiates and cocaine to more recent and emerging drugs such as methamphetamine and Ecstasy. In addition to research on illegal drugs, NIDA supports an extensive research portfolio to combat what may be the most critical and costly U.S. public health problem—tobacco use. NIDA nicotine research continues to increase knowledge about the social, economic, cultural, and biological factors that influence smoking initiation and vulnerability to nicotine addiction, and it continues to bring effective prevention and treatment approaches to the U.S. public attention. Additionally, NIDA supports research on the health consequences of nicotine as well as on the medical consequences of all illicit drugs.

Given that as of 2008 drug abuse was the greatest vector for the spread of HIV, a significant portion of NIDA research investment was spent on researching effective prevention and treatment strategies to combat HIV/AIDS and other infectious diseases. NIDA comprehensive research portfolio included studies on the causes and consequences; the prevention and treatment; and the biological, social, behavioral, and neuroscientific bases of drug abuse and addiction. NIDA was also charged with the development of medications to treat drug addiction. Additionally, NIDA supported research training and career development, science and public education, and research dissemination.

NIDA is the largest institution devoted to drug-abuse research in the world, supporting drug-abuse research through grants to scientists, primarily at major research facilities in the United States, abroad, and at NIDA Intramural Research Program (IRP).

HISTORY

Drug-abuse research and treatment was a concern of the U.S. Public Health Service from the early 1930s into the twenty-first century. The Public Health Service Hospitals at Lexington, Kentucky, and at Fort Worth, Texas, were established in 1929, and the research laboratories were established at Lexington in 1935.

NIDA was formally established in 1974 as one of three applied and basic research institutes within the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), a Public Health Service agency within the Department of Health and Human Services. The NIDA mandate was to collect information on the incidence, prevalence, and consequences of drug abuse; to improve the understanding of drugs of abuse and their effects on individuals; and to expand the ability to prevent and treat drug abuse. During this time, NIDA supported model and demonstration programs in prevention, treatment, and rehabilitation as well as basic research.

In October 1992, the drug, alcohol, and mental-health activities within the Department of Health and Human Services (NIDA, along with the National Institute on Alcohol Abuse and Alcoholism and National Institute on Mental Health), were transferred from ADAMHA to the National Institutes of Health.

FUNCTIONS

Through scientific research, NIDA built a base of information on how drugs affect people: what they do to the human body; to human behavior, thoughts, and emotions; to social relationships; and to society in general. This understanding of the biological, social, behavioral, and environmental influences that place individuals at risk for drug abuse is of great importance to prevention and treatment practitioners, to educators, and to policymakers.

NIDA has two principal goals. The first is the strategic support and conduct of research across a broad range of disciplines. The second is ensuring the rapid and effective dissemination and use of the results of that research to significantly improve

prevention, treatment, and policy as it relates to drug abuse and addiction.

To improve the ability to prevent drug abuse, NIDA concentrates on the variety of biological, behavioral, social, and environmental factors involved in vulnerability to drug abuse. This information enables NIDA to improve both prevention and treatment approaches—which are essential for overcoming the demand for drugs—and to inform effective U.S. demand-reduction policies.

Since research has shown that treatment can be an effective tool in helping some to break the addiction cycle, NIDA researches ways to improve the effectiveness of treatment and works to increase retention rates and reduce relapse rates. Through an understanding of the effects of drugs on the brain, NIDA develops more effective treatments, including medications, for specific drugs of abuse, such as cocaine and heroin, and for the toxic effects on the brain and other organs that drugs of abuse produce. NIDA has engaged in a major effort to improve research on, and its application to, services for drug-abusing pregnant and postpartum women. NIDA also seeks to develop strategies to prevent or ameliorate the consequences of drugs of abuse on the children of drug-abusing parents and continues to study the links between addiction and other diseases, including HIV/AIDS and mental disorders.

To support this array of research programs, NIDA sponsors drug-abuse research programs in the biomedical and behavioral sciences. These programs include support of pre- and postdoctoral training in medical schools, universities, and other institutions of higher education in basic, clinical, behavioral, and epidemiological research, to assure the steady supply of trained scientists. These findings are disseminated to the widest audience possible. NIDA has an extensive outreach and public education program to rapidly provide research-based information to scientists, practitioners, policy makers, and the general public. NIDA staff works closely with local community-based networks to hold town meetings at various locations across the country, as well as other major conferences, to ensure that the latest scientific information is disseminated to those working to prevent and treat drug abuse and addiction. NIDA also develops written and electronic materials for researchers, prevention practitioners, treatment practitioners, young people, parents, policy-makers, and others. Additionally, NIDA develops materials for K-12 students and teachers, as well as the general public, and funds grants with educators and scientists for the development of programs, materials, and museum exhibits. Through NIDA research dissemination programs, science-based information can then be used to educate, prevent, treat, and rehabilitate.

NIDA conducts and supports research that has as its underlying principles the goals of eliminating drug abuse, treating those whom prevention fails, increasing retention and decreasing relapse, and improving the health and well-being of all Americans, their families and their communities. Current and future directions in NIDA research can be found at http://www.nida.nih.gov/.

NIDA collaborates with other research institutes, and with other agencies and departments of the U.S. government. More information is available at the NIDA website at http://www.nida.nih.gov.

See also **U.S. Government Agencies: U.S. Public Health Service Hospitals.**

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OFFICE OF DRUG ABUSE LAW ENFORCEMENT (ODALE)

Located within the U.S. Department of Justice, the Office of Drug Abuse Law Enforcement (ODALE) was established by President Richard M. Nixon with Executive Order 11641 in January 1972. Myles J. Ambrose was appointed director of ODALE and held two other concurrent titles: special consultant to the president for drug abuse law enforcement and special assistant attorney general.

FEDERAL, STATE, AND LOCAL TEAMWORK

Complementing federal efforts directed at "high-level drug traffickers," ODALE was charged with attacking the heroin-distribution system at the street level to reduce the drug's availability there. Patterned after the Justice Department's Organized Crime Strike Forces, the ODALE program included task forces of federal, state, and local law-enforcement officers and attorneys. The full use of federal, state, and local narcotics laws, the

availability of assigned attorneys, and the use of the investigative grand jury made possible a wide range of approaches in pursuing violators.

ODALE established task forces in thirty-four cities in 1972 and encouraged citizens to "report information regarding alleged narcotics law violators in strict confidence." The federal government paid for task force equipment and operational expenses, including payments for a portion of the salaries and overtime of state and local officers. ODALE was credited with more than 8,000 narcotics arrests with a conviction rate of more than 90 percent during its 17 months of operation. Nevertheless, ODALE agents were widely criticized for conducting several drug raids involving unauthorized forcible entries into private homes and failures in identifying themselves as law officers during drug raids.

REORGANIZATION

ODALE was abolished on July 1, 1973, by Presidential Reorganization Plan No. 2 of 1973 and "those Federal operations designed to attack narcotics traffic at the street level in cooperation with local authorities" were transferred to the newly established Drug Enforcement Administration (DEA). The ODALE program was redesignated as DEA's State and Local Task Force program. ODALE's Deputy Director John R. Bartels, Jr., became the first administrator of the DEA.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy.**

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RICHARD L. WILLIAMS

OFFICE OF DRUG ABUSE POLICY

In March 1976, Congress authorized the creation of the Office of Drug Abuse Policy (ODAP) in the Executive Office of the President, with an annual budget of $1.2 million. President Jimmy Carter opened the office in March 1977 and appointed Dr. Peter G. Bourne as director.

The director of ODAP was given wide responsibilities in assisting the president with all federal drug-abuse matters, including providing "policy direction and coordination among the law enforcement, international and treatment/prevention programs to assure a cohesive and effective strategy that both responds to immediate issues and provides a framework for longer-term resolution of problems." The statutory authority included setting objectives, establishing priorities, coordinating performance, and recommending changes in organization.

During the first year of operation, ODAP conducted several international missions and worked closely with United Nations narcotics organizations. In coordinating federal drug activities, ODAP relied on biweekly discussion meetings with the heads of the principal drug agencies. Policy determination was executed through cooperative interagency study efforts. ODAP completed six comprehensive interagency policy reviews: border management, drug law enforcement, international narcotics control, narcotics intelligence, demand reduction, and drug abuse in the armed forces.

The ODAP staff coordinated preparation of President Carter's August 1977 Message to the Congress on Drug Abuse and initiated the planning for a comprehensive federal strategy to be published by the revitalized Strategy Council.

REORGANIZATION

After one year of successful operation, ODAP was abolished by Reorganization Plan No. 1 of 1977, effective March 31, 1978. Six ODAP staff members were transferred to a special drug-policy unit (Drug Policy Office) within the White House Domestic Policy Staff. The drug-policy staff continued to report to Dr. Bourne who became special assistant to the president for health issues.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy.**

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OFFICE OF NATIONAL DRUG CONTROL POLICY

The Office of National Drug Control Policy (ONDCP) was established on January 29, 1989, by Public Law 100-690 (21 USC 1504) as the drug-coordination agency for the Executive Office of the President (EOP) under President George H. W. Bush. It resulted from the Anti-Drug Abuse Act of 1988. ONDCP is responsible for coordinating federal efforts to control illegal drug abuse. It is the product of almost two decades of congressional efforts to mandate a so-called drug czar—the law providing for cabinet-level status and congressional involvement in drug-control policy. ONDCP oversees the international and domestic antidrug functions of all executive agencies and ensures that such functions sustain and complement the government's overall antidrug efforts.

ONDCP's overarching purpose is to set the objectives, priorities, and policies for drug control in the United States. Its stated mission is to decrease the manufacture, distribution, and use of illegal drugs; to combat the violence and illegal activities associated with illicit drugs; and to ameliorate or mediate drug-related health problems.

THE DIRECTOR

ONDCP is led by a director (commonly referred to as the drug czar) with cabinet-level rank (executive level 1), two component deputies (supply reduction and demand reduction), and one associate director (state and local affairs), all appointed by the president with the advice and consent of the Senate. The director has a broad mandate for establishing policies, objectives, and priorities for the National Drug Control Program. Serving as the president's drug-control adviser and as a principal adviser to the National Security Council (NSC), the director has extraordinary management tools available to influence national drug-control efforts.

ONDCP is required to produce an annual National Drug Control Strategy for the president and Congress, and is responsible for overseeing its implementation by the federal departments and agencies. Included are an annual consolidated National Drug Control Program budget and the director's certification that the budget is adequate to implement the strategy's objectives. In addition to the strategy and program oversight, the director has two other legislated management tools: (1) approval of reprogramming of each agency's drug funds and (2) formal notification to the involved agency and the president when a drug-program agency's policy does not comply with the mandated strategy. The director also recommends changes in the organization, management, and budgets of departments and agencies engaged in the drug effort, including personnel allocations.

Reflecting congressional desire to participate in drug policy, the director must represent the administration's drug policies and proposals before Congress. Additionally, the authorizing legislation specifically allows Congress access to "information, documents, and studies in the possession of, or conducted by or at the direction of the Director" and to personnel of the office.

ORGANIZATION AND AUTHORITY

ONDCP's authority to provide direction to diverse federal departments and agencies is based on a program-management structure known as the National Drug Control Program. The ONDCP program and budget authority coexist with the line authority of the cabinet departments and with the president's annual budget process (directed by the Office of Management and Budget). The structure for the parallel drug-control system is created by designating National Drug Control Program agencies, defined as "any department or agency and all dedicated units thereof, with responsibilities under the National Drug Control Strategy." The designated federal departments and agencies have special program and budget responsibilities to the director of ONDCP. ONDCP's broad coordination authority

over budgets and program activity also presents extraordinary opportunities for conflict with the existing line of authority in the departments and agencies. Simultaneously, ONDCP receives congressional and press criticism regarding lack of influence over operating activities.

POLICY DEVELOPMENT AND COORDINATION

The continued success of the complex drug-policy system depends on the continuing high priority of drug programs and seeking of widespread understanding and endorsement of the goals and objectives for the national program. An element essential to effective communication is a public document that explains the program's strategy, goals, and responsibilities—including a dynamic process of evaluating results and updating U.S. strategy.

The annual National Drug Control Strategy and accompanying budget summary are developed annually by the Office of the President. It contains three areas of emphasis: (1) stopping use before it starts, (2) intervening and healing America's drug users, and (3) disrupting the market. For fiscal year (FY) 2009 the drug budget totals $14.1 billion, representing an increase of 3.4 percent or $459 million from the previous budget. The administration also has a pending request for $2385.1 million for counternarcotics support to Central America and Mexico as a result of the Merida Initiative. Fostering improved security cooperation between the United States, Mexico, and Central America is the focus of the Merida Initiative, which is a multiyear $1.4 billion program aimed at decreasing cross-national crime. In FY 2008 ONDCP requested a budget supplement of $385.1 million to launch the program. The supplemental request for Merida in FY 2009 is $432.2 million.

Twelve agencies work together under the budget auspices of ONDCP. The drug-control programs funded and supported through the Departments of Education, Health and Human Services, Interior, Small Business Administration, and Veterans Affairs are dedicated to demand reduction activities, whereas the Departments of Defense, Homeland Security, Justice, State, Transportation, and Treasury focus on supply reduction activities. The ONDCP is involved in both demand and supply reduction.

The National Drug Control Strategy acknowledges that no single tactic will solve the drug problem. Therefore, the annual strategies call for improved and expanded treatment, prevention, and education; increased international cooperation; aggressive law enforcement and interdiction; expanded use of the military; expanded drug intelligence; and more research.

ORGANIZATION FOR COORDINATION

ONDCP has established a drug-control management agenda, including federal coordinating mechanisms and senior-level management committees and working groups. The organization of ONDCP includes staff for supply reduction, demand reduction, and state and local affairs. ONDCP working groups and committees coordinate the implementation of the policies, objectives, and priorities established in the National Drug Control Strategy.

PROGRAMS

Stopping Use Before It Starts. The $1.6 billion budget is dedicated to prevention, education, and outreach efforts designed to deter American youth from initiating drug use. Some of the pivotal programs are Safe and Drug-Free Schools and Communities, the National Youth Anti-Drug Media Campaign, Drug-Free Communities, and Student Drug Testing.

Intervening and Healing America's Drug Users. More than $3 billion of the drug budget is earmarked for drug-abuse interventions and treatment programs. Screening, Brief Intervention, Referral, and Treatment (SBIRT) activities are local (state, territory, and tribe) grant programs located within medical settings (such as community health centers and emergency rooms) where health providers screen and assess persons for substance-abuse-related problems. Those who are positively identified are afforded brief interventions and referred, as necessary, for higher levels of care. The Healthcare Common Procedure Coding System (HCPCS) has instituted two codes specific to alcohol and drug screening and brief intervention (SBI). SBI has demonstrated efficacy for reducing substance use, and approval of the HCPCS codes will allow state Medicaid dollars to pay for SBI programs. Access to Recovery (ATR) vastly expands access to treatment through the use of smaller

community-run or faith-based programs. ATR programs use voucher systems to create a means of payment for persons who would not otherwise be able to afford help. Family, adult, and juvenile drug courts offer grant-based programs that provide participants with the ability to participate in treatment programs as an alternative to incarceration when possible.

Disrupting the Market. These funds, totaling over $8 billion, are used for emergency designations such as the operations occurring in Afghanistan, and for numerous other programs designed to disrupt the illegal drug trade worldwide. The funds are used for interdiction operations at national borders, and for improving mechanisms for detecting, tracking, and interrupting drug manufacture and trafficking.

The federal drug-control agencies and departments are represented on the various working groups and committees, along with ONDCP staff. The organizational structure includes the following coordinating mechanism.

ONDCP Supply Reduction Working Group. Chaired by the ONDCP deputy director for supply reduction, this working group includes three committees:

- The Border Interdiction Committee. Coordinates strategies and operations aimed at interdicting drugs between source and transit countries and at U.S. borders.
- The Public Land Drug Control Committee. Coordinates federal, state, and local drug-control programs (primarily marijuana eradication efforts) on federal lands.
- High-Intensity Drug Trafficking Area Program (HIDTA). Coordinates drug law enforcement activities in designated areas, including federal, state, and local enforcement task forces and intelligence activities, which have particularly significant drug trafficking problems that transcend their geographic areas and impact other parts of the nation. HIDTA directs additional federal resources to those areas with the goals of reducing, and eventually eliminating, trafficking and its attendant problems. HIDTA partners with local and regional law enforcement agencies in order to design and implement programs specifically tailored to the needs of the area, using a multimodal approach to eliminate the sources of manufacture, distribution, and transport and other criminal activities while also addressing issues of treatment and prevention.

ONDCP Demand Reduction Working Group. Chaired by the ONDCP deputy director for demand reduction, this working group coordinates policies, objectives, and outreach activities for treatment, education and prevention, workplace, and international demand reduction.

Research and Development Committee. Chaired by the director of ONDCP, this committee provides policy guidance for the research and development (R&D) activities of all federal drug-control agencies, including the following R&D working committees:

- The Data Committee. Improves the relevance, timeliness, and usefulness of drug-related data collection, research studies, and evaluations of both demand-related and supply-related activities.
- The Medical Research Committee. Coordinates policy and general objectives on medical research by federal drug-control agencies and promotes the dissemination of research findings.
- The ONDCP Science and Technology Committee. Chaired by the ONDCP chief scientist, the committee is responsible for the oversight of counterdrug research and development throughout the federal government.

RELATED POLICY ACTIVITIES

The Counterdrug Technology Assessment Center, established by Public Law 101-509 in 1991, provides oversight of the federal government's counternarcotics R&D activities. ONDCP's chief scientist is responsible for defining scientific and technological needs for federal, state, and local law enforcement agencies, and for determining feasibility and priorities. The chief scientist also coordinates the technology initiatives of federal civilian and military departments, including research on substance abuse addiction and rehabilitation.

ONDCP works with the NSC, chairing the Policy Coordinating Committee for Narcotics to

oversee coordination among agencies with law enforcement and national security responsibilities. The director also participates in meetings of the Domestic Policy Council, which reviews the annual drug control strategy before it goes to the president.

ONDCP's state and local affairs staff have traditionally sought wide public involvement in developing and implementing drug policy at all levels of government. The ONDCP sponsored several national conferences on state and local drug policy during 1990 and 1991 to highlight successful state and local programs, seek input on the national strategy, and inform participants of funding and initiatives available to them. ONDCP staff coordinated with both the White House Office of National Service and the president's Drug Advisory Council in encouraging private-sector and state and local initiatives for drug prevention and control.

ONDCP also provides administrative support to the president's Drug Advisory Council. With 32 private citizens as members, the Drug Advisory Council focuses on private-sector initiatives to support national drug-control objectives, and it assists the ONDCP. The advisory council is financed by private gifts.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; U.S. Government: The Organization of U.S. Drug Prevention Policy.**

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SPECIAL ACTION OFFICE FOR DRUG ABUSE PREVENTION (SAODAP)

The Special Action Office for Drug Abuse Prevention (SAODAP) was created by Executive Order of President Richard M. Nixon on June 17, 1971, as a response to public concern about drug abuse, particularly heroin addiction. SAODAP was given legislative authority by the Drug Abuse Office and Treatment Act on March 21, 1972. The formation of SAODAP represented the first attempt to establish a stable focus within the federal government for the coordination of the many facets of U.S. drug policy, including law enforcement, border control, control of selected medicines, treatment, prevention, education, and research.

More than twenty agencies, offices, and bureaus within the U.S. government were responsible for activities relating to drug problems. Yet there was no evident central authority other than the president. Congress and the public seemed eager to be able to hold accountable the head of one agency who, unlike the president, could be asked to testify before Congress—a "drug czar." Although the term "drug czar" was popularly used, and it was expected that the person holding the office would exert power over the various

agencies dealing with both law enforcement (supply side) and treatment and prevention (demand side) aspects of the problem, neither the president nor the Congress were entirely comfortable with delegating such broad authority to only one individual.

The legislation submitted to Congress by the White House, which finally emerged from debate, gave SAODAP unprecedented authority over demand side activity—treatment, prevention, education, research—wherever these were carried out within the federal government. However, its mandate with respect to drug-control agencies such as the U.S. Customs Bureau, which reported to the Secretary of the Treasury, and the Bureau of Narcotics and Dangerous Drugs, which reported to the Attorney General, was limited to coordination. SAODAP was also charged with developing a formal, written, national strategy for drug-abuse prevention. To head the new office, President Nixon appointed Dr. Jerome H. Jaffe, then a professor of psychiatry at the University of Chicago and director of the Illinois Drug Abuse Programs. Dr. Jaffe, who had helped the White House develop its response to heroin use in Vietnam, was also appointed special consultant to the president on narcotics and dangerous drugs.

A primary goal of SAODAP, stated at the press conference that announced the new office, was to make treatment so available that no addicts could say they committed crimes because they could not get treatment. Although the Bureau of Narcotics and Dangerous Drugs (BNDD) had estimated that there were about a half million heroin users in the United States, in mid-1971 the true extent of the drug-abuse problem was unknown. The estimating techniques that were developed in the 1970s—the National Household Survey on Drug Abuse, the DAWN system (or Drug Abuse Warning Network), and the High School Senior Survey—did not yet exist, but the rising rate of heroin-related deaths in several major cities and the thousands of addicts waiting for treatment because there was not enough treatment capacity gave stark evidence for the growing size of the heroin problem. There were drug overdose (OD) deaths among U.S. troops in Vietnam also. Surveys generally indicated widespread drug use among U.S. servicemen in Vietnam, with the extent of the problem estimated at 15 to 30 percent, but it was not known if these estimates were of drug users or of addicts.

In addition to the mandate to coordinate all the demand side drug-abuse activities of the federal bureaucracy so as to reduce overlap and redundancy and to expand treatment capacity, some of the additional tasks of the office included overseeing and coordinating the Vietnam drug-abuse intervention; creating a new federal agency with competence to develop national policy; creating the data systems by which the effectiveness of national policy could be evaluated; creating a science base so that research might lead to better ways to treat and prevent addiction; and developing a formal, written National Strategy for drug-abuse treatment and prevention.

Four major policy changes helped the agency achieve its objectives. The first was made by the president when the Vietnam testing and treatment program was initiated: Drug use was no longer a court-martial offense. The second was having the federal government take responsibility for developing and funding treatment. The third made methadone-maintenance treatment, already being used for 20,000 people, an established and acceptable treatment method rather than an experiment. The fourth had to do with changes that were made in the thinking, language, and means by which treatment was supported.

A central effort for SAODAP was the expansion of treatment capacity, increasing not only the number of programs, but also their actual capacity and geographic distribution. In addition, recipients of funding for treatment programs became accountable for what they provided, such as the number of treatment slots and the type of treatment. While legitimizing methadone-maintenance treatment and developing regulations for its use were highly visible and highly controversial activities, they were only incidental to the overall mission of making effective treatment central to the nation's response to the drug problem. Within the first 18 months of SAODAP's efforts, the number of communities with federally supported drug-treatment programs increased from 54 to 214, and the number of programs grew to almost 400. More federally supported treatment capacity was developed within two years than over the previous fifty years.

Some of the other projects SAODAP initiated, funded, or grappled with were the Vietnam drug intervention and the Vietnam drug intervention follow-up study; the development of confidentiality regulations to protect the medical records of people seeking treatment; funding clinical research on new pharmacological treatments for drug dependence; initiating with other agencies projects such as treatment alternatives to street crime (TASC), research centers for clinical and basic research on drug abuse and addiction, the Career Teachers program that incorporated drug abuse into medical school curricula, and a National Training Center. SAODAP introduced formula or block grants that gave money through the National Institutes on Mental Health (NIMH) to the states for treatment and prevention programs; it also introduced management concepts and language into treatment systems. SAODAP played a major role in improving drug-abuse treatment in the Veterans Administration; establishing laboratory standards for urine-testing facilities; and initiating several of the epidemiological tools that continue to shape policy, such as the National Household Survey of Drug Abuse and the Drug Abuse Warning Network (DAWN) system. Many of the programs and activities developed with interagency cooperation were implemented by the agencies involved in the collaboration. Many of the activities are ongoing in the mid-1990s. SAODAP also produced the first written national strategy, entitled "Federal Strategy for Drug Abuse and Drug Traffic Prevention."

Since the baseline funding for drug-abuse treatment, prevention, and research was so low in 1971, the new resources given to SAODAP for the task represented a manyfold increase—and in some instances were the very first resources available for the purpose. The same legislation that authorized SAODAP provided for the establishment of the National Institutes on Drug Abuse (NIDA); in addition, the resources and policies for an invigorated research effort were put into place over the three budgetary cycles that preceded NIDA's creation. Dr. Robert Dupont, who succeeded Dr. Jaffe as director of SAODAP, became the first director of NIDA. Dr. Peter Bourne and Mr. Lee Dogoloff, both of whom worked at SAODAP during the first two years, later became key advisors on drug policy to President Jimmy Carter.

A noted researcher, Dr. Solomon Snyder, credits the SAODAP support he received with enabling him to discover the opiate receptor a year or two later. This discovery forms the basis for much of the neuroscience research into understanding the biology of drug dependence.

SAODAP was able to change the national response to illicit drug use by developing an infrastructure for treatment that is largely still in place, one that recognizes the heterogeneity of the drug-using population, their need for several different types of treatment, and the need for research on the efficacy of treatment. For a brief period after SAODAP's mandate expired in 1975, drug-abuse policy was coordinated by a smaller office within the Office of Management and Budget (OMB) under President Gerald R. Ford, and then by the Drug Abuse Policy Office within the White House under presidents Jimmy Carter and Ronald W. Reagan. However, until President George H. Bush established the Office of National Drug Control Policy (ONDCP), there was no formal agency with substantial authority for coordinating federal drug policy.

See also **Industry and Workplace, Drug Use in.**

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SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION (SAMHSA)

The Substance Abuse and Mental Health Services Administration (SAMHSA), established by Congress on October 1, 1992 (Public Law 102-321), works with states, communities, and organizations to strengthen the national capacity to provide substance abuse prevention, addiction treatment, and mental health services for people experiencing or at

risk for mental health and substance abuse disorders. The SAMHSA fiscal year 2009 budget was approximately $3.2 billion; it employed a staff of approximately 550. In 2008 the SAMHSA Administrator was Dr. Terry Cline, and the Deputy Administrator was Dr. Eric Broderick. The Agency houses three Offices: Office of Applied Studies, Office of Policy, and Office of Program Services; and three program Centers: Center for Mental Health Services (CMHS), Center for Substance Abuse Prevention (CSAP), and Center for Substance Abuse Treatment (CSAT). (More specific information can be found at the respective Web sites for each center.)

Because the main objective of SAMHSA is to continually expand and improve the quality and availability of mental health, substance abuse prevention and treatment, and behavioral health (combined mental health and substance abuse) services throughout the United States, the organization developed grant funding programs. Grant portfolios include both block and discretionary grants. Block grants enable states to maintain and enhance their substance abuse and mental health services. Targeted Capacity Expansion grants provide resources to communities to identify and address emerging substance abuse and mental health service needs at their earliest stages. The SAMHSA Knowledge Application Program grants implement and assess new community-based prevention and treatment methods. Grant funds are awarded through CMHS, CSAP, and CSAT.

The SAMHSA Center for Mental Health Services (CMHS) works to improve the availability and accessibility of high-quality care for people with or at risk for mental illnesses as well as for their families by creating a nationwide community-based mental health service infrastructure. CMHS education programs are helping to end the stigma associated with these illnesses. While the largest portion of the Center's annual budget supports the Community Mental Health Services Block Grant Program to states, CMHS also supports grant programs to develop and apply knowledge about best community-based practices designed to serve adults with serious mental illnesses and children with serious emotional disturbances. The Center also collects and analyzes national mental health services data to help inform future services decision-making.

The Center for Substance Abuse Prevention (CSAP) is the national focal point for the identification, promotion, and dissemination of effective strategies to prevent drug and alcohol abuse and tobacco use. CSAP programs identify prevention strategies—such as targeted family and community strengthening—that work best for specific populations at risk of substance abuse. Program approaches emphasize both cultural relevance and competence. The Center oversees federal workplace drug-testing programs as well as state implementation of the Synar Amendment, which prohibits youths under age 18 from purchasing tobacco. In addition CSAP supports the National Clearinghouse for Alcohol and Drug Information (NCADI), the largest information source on substance abuse research, treatment, and prevention in the nation. CSAP also oversees four grant programs (State Incentive, Drug-Free Community, HIV, and Methamphetamine).

The Center for Substance Abuse Treatment (CSAT) works to enhance the quality of substance abuse treatment services and to ensure that services are available to all who need them. It supports the identification, evaluation, and dissemination of proven effective treatment services. CSAT administers the state Substance Abuse Prevention and Treatment block grant and undertakes knowledge development, education, and communications initiatives that promote best practices in substance use/abuse treatment and intervention. The CSAT Targeted Capacity Expansion Program—and its specialized program focused on HIV/AIDS services—helps communities respond rapidly to emerging local drug use trends. In addition to the Co-Occurring Center for Excellence, CSAP oversees many programs including Access to Recovery (ATR), Partners for Recovery (PFR), the Knowledge Application Program (KAP), the National Center on Substance Abuse and Child Welfare (NCSACW), National Alcohol and Drug Addiction Recovery Month, the Substance Abuse Treatment Facility Locator, Medication Assisted Treatment (MAT), the Recovery Community Services Program, Addiction Technology Transfer Centers, Practice/Improvement Collaboratives Program, Persistent Effects of Treatment Studies, CMHS/CSAT Spending, Organization, and Financing Treatment Services, the Treatment Improvement Exchange Forum, As You Age, the Do the Right Dose program for discouraging elders from

abusing prescription pain medications, and the *SBIRT* programs. CSAP also funds programs at the state and local levels to improve and expand substance abuse treatment services via Substance Abuse Treatment and Prevention (SAPT) block grants.

While SAMHSA's Office of the Administrator and Office of Program Services are primarily administrative in nature, the Office of Applied Studies (OAS) has program authority to gather, analyze, and disseminate data on substance abuse practices in the United States. It collects data on alcohol, tobacco, marijuana, and other drug abuse; drug-related emergency department episodes; medical examiner cases; and the national substance abuse treatment system. OAS directs the annual National Survey on Drug Use and Health (NSDUH), the Drug Abuse Warning Network (DAWN), and the Drug and Alcohol Services Information System (DASIS), among others. Through these studies, SAMHSA identifies trends in substance abuse and mental health care. OAS also coordinates evaluation of models developed through SAMHSA knowledge development and application programs.

Other SAMHSA initiatives include the 15+ Make Time To Listen . . . Take Time to Talk program, the As You Age public education campaign, the Building Blocks for a Healthy Future early prevention program, the Fetal Alcohol Spectrum Disorders (FASD) Center, the nationwide Helping America's Youth effort led by First Lady Laura Bush, the Mental Health Services Locator searchable online directory, the National Strategy for Suicide Prevention (NSSP), the Older Americans Technical Assistance Center, Partners for Recovery (PFR) support and technical resource system, Projects for Assistance in Transition from Homelessness (PATH) formula grants, the Recovery Community Services Program (RCSP) peer-to-peer recovery support services, Recovery Month programs, Safe Schools/Healthy Students (SS/HS) Initiative, Systems of Care grants and community/local programs, and the Knowledge Application Program (KAP) initiative, among many others. (A more complete listing of initiatives and more information about those listed can be found at the SAMHSA Web site.)

SAMHSA comes up with new program ideas in varying ways. Some are developed by SAMHSA leadership and staff; others result from congressional mandate. Still other grow from Center-sponsored meetings that highlight empirically validated intervention models ripe for replication. Some new program directions originate at the state and local levels, some from SAMHSA and Center National Advisory Councils, and some from the research community.

SAMHSA programs bring new science-based knowledge to community-based prevention, identification, and treatment programs for mental and substance abuse disorders. Results are evident in improved approaches to addiction treatment, substance abuse prevention, and mental health services at the federal, state, and community levels. Equally important, the results are obvious in the improved quality of people's lives.

See also **Treatment: An Overview; Treatment, Behavioral Approaches to: An Overview.**

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U.S. CUSTOMS AND BORDER PROTECTION (CBP)

Housed within the Department of Homeland Security, the U.S. Customs and Border Protection (CBP) is tasked with securing the entirety of the U.S. border from human and drug smuggling, terrorism, and illegal migration (both immigration and emigration), as well as overseeing international trade and travel. The CBP guards the 7,000 miles of border between the United States and Canada and Mexico, in addition to the California coastline and the waters surrounding Florida. The U.S. Coast Guard works with the CBP in patrolling the 95,000 miles of maritime border surrounding the United States.

Of CBP's more than 44,000 staff, over 13,000 are Border Patrol or CBP Air and Marine agents, while some 20,000 are CBP officers and agriculture specialists. In addition, CBP employs the largest number of canine patrol teams in the United States. CBP Officers are stationed at official points of entry into the country (also called CBP Stations), and Border Patrol agents are tasked with the prevention of illegal entry of contraband and persons between these official border-crossing locations. CBP also conducts a wide range of statutory and regulatory activities, ranging from interdicting and seizing contraband entering the United States to intercepting illegal exports of high-technology items. Put simply, U.S. Customs and Border Protection serves as the single unified agency responsible for protecting the country's borders.

CBP'S ROLE IN DRUG ENFORCEMENT

CBP is both a leader and a major player in stopping drug contraband from entering the United States. CBP's inspection and control function is directed at stopping illegal entry of drugs and other contraband, while also accommodating the normal flow of persons and cargo entering the United States and enforcing export laws. More than $9.2 billion of the annual federal budget is allocated to interrupting illegal drug trade, and the Department of Homeland Security, the U. S. Coast Guard, and CBP play major roles in the interdiction of contraband substances along the borders of the country. The Merida Initiative, which was established in February 2008, is a $1.4 billion multiyear program designed to expand the cooperative relationship between Central America, Mexico, and the United States. The intention of this program is to dramatically decrease the incidence of cross-border drug trafficking and other international crimes. In fiscal year 2008, $385.1 million will specifically target drug-related activities; in fiscal year 2009, the budget will be increased to $550 million, with $432.2 million targeted specifically toward work with Mexico and Central America. Approximately $570 million of the 1993 CBP budget was related to antidrug operations.

As the lead federal agency at U.S. ports of entry, CBP inspects individuals, conveyances, mail, and cargo entering the United States by land, sea, and air. It has broad search and seizure authority at the U.S. borders and handles enormous workloads. On a typical day, for example (using 2006 data), CBP processes roughly one million passengers and pedestrians, 327,000 privately owned vehicles, 71,000 containers, and 85,000 shipments of goods and cargo. CBP operates a comprehensive computerized border information system and uses other domestic and international drug-intelligence networks. The agency's efforts are prioritized to target the illegal traffic in precursor chemicals, to improve interdiction intelligence, and to engage in special

high-intensity enforcement operations, particularly along the southwest border. More than 60 people are arrested at points of entry every day, and nearly 3,000 are caught attempting to enter the country illegally. In addition, on an average day CBP seizes 1,800 pounds of narcotics at border crossings, nearly 4,000 pounds of narcotics between legal border crossing areas, more than $150,000 in illicit or undeclared currency, and about $650,000 in fraudulent commercial merchandise at border entry points. In order to achieve this mission, approximately 1,250 human-canine pairs, 6,000 vehicles, 260 aircraft, 200 watercraft, and 200 equestrian patrols are utilized.

APPROACHES TO INTERDICTION

As a large, multipurpose border-control agency, CBP has considerable flexibility in determining the most effective means to meet its responsibilities. The traditional approach involves the physical presence of uniformed officers at the border to detect and seize violators and contraband. CBP emphasizes the development of the best possible detection capabilities and information systems to facilitate identification of persons who might pose a terrorist threat. These include the Advance Passenger Information System (APIS), the Student and Exchange Visitor System (SEVIS), and U.S. Visitor and Immigrant Status Indication Technology (US-VISIT). The Automated Targeting System (ATS) and the Automated Export System (AES), along with the Advance Electronic Information regulations that were part of the Trade Act of 2002, facilitate the identification of cargo or goods that could pose a threat.

The CBP became part of the Department of Homeland Security following the terrorist attacks on September 11, 2001. Since then, it has utilized its Office of Intelligence and the National Targeting Center (NTC) to increase its capabilities for processing and synthesizing information and improve its tactical accuracy in identifying suspicious cargo prior to its arrival at a U.S. border. CBP also works closely with the U.S. Coast Guard and U.S. military forces in providing surveillance, interception, and deterrence against drug smuggling by air and sea. CBP is working actively with Mexico and Canada to facilitate the smooth flow of legal travel and trade activities across these borders, while also intensifying cooperative efforts aimed at preventing the smuggling of contraband, weapons, drugs, and humans.

See also **Anslinger, Harry Jacob, and U.S. Drug Policy; Border Management; Drug Interdiction; International Drug Supply Systems; Operation Intercept; Zero Tolerance.**

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U.S. PUBLIC HEALTH SERVICE HOSPITALS

In 1929, President Herbert C. Hoover signed a law enacted by the U.S. Congress to establish two federal institutions for treatment of narcotic addiction. The principal purpose of the institutions was to confine and treat persons addicted to narcotic

drugs who had been convicted of offenses against the United States. However, the law also provided for voluntary admission and treatment of addicts who were not convicted of any offense. The two institutions were named U.S. public health service hospitals. One was opened in 1935 at Lexington, Kentucky, and the other in 1938 at Fort Worth, Texas. The Lexington hospital had a capacity of 1,200 patients; the Fort Worth hospital could accommodate 1,000 patients. From opening to closure in 1974, the hospitals admitted over 60,000 narcotic addicts; because of readmissions, the total admissions exceeded 100,000. Most of the admissions were voluntary. The term *narcotic addiction* has been replaced in modern diagnostic terminology by the term *opioid dependence*, but in this discussion the older term is retained because it was regularly used during the era reviewed here. The history of the hospitals is divided into three periods.

FIRST PERIOD, 1935–1949

From the start, the hospitals were designed to treat not only the physical dependence but also the mental and emotional problems thought to be related to addiction. This was an advanced conception, for treatment of narcotic addiction until then had been focused almost exclusively on the physical dependence. The initial treatment programs at both hospitals emphasized residence in a drug-free environment for at least six months, during which time the patient could not only recover from the physical dependence but perhaps also overcome the mental difficulties or learn to adapt to them without using drugs. While all patients received psychological help in the form of encouragement and persuasion, only small numbers received formal psychotherapy. That was because few of the staff were trained in psychotherapy. All patients considered physically able had work assignments, and all had access to educational and vocational services, recreation, and religious activities. Treatment of voluntary patients was hindered because most left during or shortly after withdrawal treatment (often to return to lower doses of their drug—before readmission). In 1948, the research division of the Lexington hospital reported that a new synthesized narcotic drug called methadone was effective in the treatment of opiate withdrawal. Methadone substitution followed by a gradual decrease of its dose subsequently became the standard treatment for morphine and heroin withdrawal in the United States. Also in 1948 the research division of the Lexington hospital was administratively separated from the hospital, renamed the Addiction Research Center (ARC) and made a part of the National Institute of Mental Health (NIMH).

SECOND PERIOD, 1950–1966

After World War II, the prevalence of heroin addiction in the United States markedly increased. Heroin replaced morphine as the primary narcotic used. Annual admissions to the two hospitals doubled from the 1940s to the 1950s. The prewar addicts differed from their postwar counterparts. More of the postwar addicts came from large cities, and more came from minority groups (mainly black and Hispanic).

While residence in a drug-free environment continued as a major feature, new psychosocial treatments were made a part of the program. Psychoanalytically oriented psychotherapy was offered, but few patients seemed willing or able to engage in this form of therapy. Group therapy, however, seemed more acceptable, and most patients participated in it to some extent. Influenced by new concepts of the therapeutic community, staff members tried to improve the quality of the patients' psychosocial experience in the hospital.

THIRD PERIOD, 1967–1974

In 1967, a research mission was assigned to the two hospitals, and each was renamed a National Institute of Mental Health Clinical Research Center. Before the research mission could be developed, however, a new clinical mission was assigned to the two institutions. The Narcotic Addict Rehabilitation Act (NARA), enacted in 1966, provided for the civil commitment of addicts instead of prosecution on a criminal charge, or sentence after conviction, or by petition with no criminal charge. The law authorized the Public Health Service to enter into contracts with any public or private agencies to provide examination or treatment of addicts committed under the NARA, but it was decided to use the two clinical research centers to implement the act quickly. Admission of prisoners and voluntary patients was phased out, and the centers concentrated on service to the NARA patients.

From 1967 through 1973, over 10,000 NARA patients were admitted to the two centers. Nearly all were admitted under the provision of the law that permitted commitment with no federal criminal charge.

The NARA civil commitment seemed a promising way to eliminate the problem of voluntary patients who signed out prematurely. In practice, it only reduced the problem. Patients learned that commitment could be avoided or terminated if they refused to participate in treatment activities or engaged in disruptive or antagonistic behavior. Only about one-third of the NARA patients completed a six-month period of institutional treatment.

The NARA program led to the closure of the two centers. As more contracts were made with local facilities for examination and treatment of NARA patients, admissions to the two centers decreased. In addition, a new federal program, started in the late 1960s, of grants to states and communities for drug-abuse treatment programs made the centers less needed. The Fort Worth Center was closed in 1971 and the Lexington Center in 1974. The facilities were transferred to the Federal Bureau of Prisons and were converted into correctional institutions.

HISTORIC ROLES OF THE HOSPITALS

For approximately three decades, from the 1930s into the 1960s, the two Public Health Service hospitals were almost the only institutions in the United States engaged in the study and treatment of narcotic addiction. They became international centers of expertise. Staff members published many reports on the psychosocial characteristics of the addicts, the treatment programs, treatment outcomes, and related topics. Many clinicians and investigators who worked at Lexington and Fort Worth left these institutions to become leaders in treatment of or research on narcotic addiction at other locations. Despite great efforts, however, the hospitals failed to develop an enduring cure for narcotic addiction. Hospital treatment often produced a temporary remission in the addiction, but relapse within a year was the typical outcome.

See also **Opioid Dependence: Course of the Disorder Over Time; Wikler's Conditioning Theory of Drug Addiction.**

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JAMES F. MADDUX

VALUES AND BELIEFS: EXISTENTIAL MODELS OF ADDICTION. Existential models of addiction focus on the sense of self of drug users, and the meanings the experience of drug use has for the individual. According to one existential theory of drug dependence certain individuals are "addiction prone" because of a disordered emotional state and pathological personality factors (Greaves, 1980). Other accounts focus on the values, attitudes, and beliefs of drug users. For example, psychologists have found that problem drinkers and alcoholics anticipate greater benefits and more powerful effects from drinking than do other drinkers. These beliefs precede actual drinking experiences (Miller et al., 1990). Khantzian has proposed that some users are predisposed to addiction because they take drugs to self-medicate emotional distress and psychiatric problems such as depression (1985). According to Peele, the individual becomes addicted to a substance because it fulfills essential intrapsychic, interpersonal, and environmental needs (1985).

CULTURAL BELIEFS IN ADDICTION

Cultural beliefs, norms, and values are intimately connected with existential experiences. They are among the most powerful determinants of the patterns of alcohol and drug use (Heath, 2000). Early work on cultural variations in drinking behavior in the United States found that moderation was inculcated as an early and firm cultural style among Mediterranean ethnic groups, Jews, and the Chinese (Barnett, 1955; Hanson, 1995). Such cultural socialization incorporates beliefs about the power of alcohol and the nature of those who overindulge or misbehave when drinking. Groups such as the Irish that invest alcohol with the power to control and corrupt their behavior were found to have high levels of alcoholism. In contrast, Jews, Italians, and Chinese believed that those who drink to excess are displaying poor self-control and/or psychological dependence, rather than responding to the power of the alcohol itself (Vaillant, 1983; Glassner & Berg, 1984; Bales, 1946). MacAndrew and Edgerton's influential book *Drunken Comportment* (1969) emphasized cross-cultural variation in intoxicated behavior, observing that in some cultures drunkenness operated as an accepted excuse for bad behavior whereas in others behavioral norms for sober and drunken states were similar.

Other work has stressed the need to recognize the multiple effects of socioeconomic status, gender, education, generation, age, and occupation rather than treating ethnicity or cultural background as simple determinants of views about alcohol and drinking behavior (Ames & Rebhun, 1996; Dawson, 1998). Ethnic categories need to be carefully employed; for example, while it is possible to generalize that Asian Americans generally drink less than white Americans and that there are relatively few alcohol problems among Asian Americans, Japanese Americans appear to have relatively high rates of heavy drinking (O'Hare, 1995). Dwight Heath, one of the key scholars of alcohol and culture, has observed that ethnicity has been used too loosely in alcohol studies, in ways that overlap with

nationality, religion, race, and cultural background (1998). Cultural identities should not be regarded as uniform and static entities; their content and salience change over time, location, and social context (Heath, 2000).

The existential and cultural approaches to addiction, along with other social constructionist frameworks, are often assumed to be alternatives to biological models and incompatible with explanations that draw on the neuropharmacology of different drugs. However, the integration of the cultural and the biological is a key issue in addiction and drug research (Kushner, 2006). The question of how cultural beliefs interact with pharmacology requires further research. Steele and Joseph's notion of "alcohol myopia" provides one starting point as it attempts to explain how a single drug can have diverse behavioral effects (1990; Room, 2001). It proposes that alcohol intoxication restricts attention to the most immediate cues in a setting, a cognitive short-sightedness that can produce a range of effects from altruism and conviviality to violence. Thus, the effects of alcohol vary from person to person, occasion to occasion, and culture to culture, depending on the cues that are relevant.

Another pressing question is how to conceptualize the interaction of cultural and biological factors in the influential "dependence syndrome" model of addiction developed by Griffith Edwards. Edwards argues that as a syndrome, rather than a disease, alcohol dependence should be thought of as something that is not all or nothing, but something that can be experienced in varied degrees, with a collection of signs and symptoms that are not definitive but may vary over time and cultural location (2003). Syndromes of dependence thus have multiple triggers and pathways informed by what Kushner has called "cultural biology" (2006).

VALUES

In general, scientific and scholarly accounts of addiction have distanced themselves from claims about the relationship between values, morals, and excessive drug and alcohol use. Indeed, such perspectives are seen as impeding the development of an objective science of addiction. Because pharmacologically-based theories often emphasize the potency of the drug and the altered physiology and neurology of the addict as the basis of compulsion, they tend to exclude the role of values in influencing people's choices about drugs.

Peele has challenged this approach, claiming that people become addicted due to a failure of other values that maintain ordinary life involvements (1987). In Peele's view, personal values influence whether people use drugs, whether they use them regularly, whether they become addicted, and whether they remain addicted. These values include prosocial behavior (including achievement, concern for others, and community involvement), self-awareness and intellectual activity, moderation and healthfulness, and self-respect. According to Peele, the explicit values people cite as reasons for giving up addictions to cocaine, alcohol, and nicotine are evidence of the importance of values in drug use (Reinarman et al., 1991). However, the protective values Peele cites such as achievement, self-awareness, and self-respect are themselves culturally-specific ideals of individual virtue. The relationship between these values and different cultural beliefs about alcohol is not clear.

See also **Alcoholism: Origin of the Term; Chinese Americans, Alcohol and Drug Use among; Jews and Alcohol.**

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VENTRAL TEGMENTAL AREA. The ventral tegmental area, (VTA), is a very important brain area in the field of drug abuse. It is one of only two main areas that contain dopamine cell bodies. The mesolimbic dopamine pathway originates in the VTA. Dopamine neurons in the VTA project to areas of the brain associated with emotion and motivation, the so-called limbic areas. However, the projection to the nucleus accumbens is the most important in understanding the action of drugs of abuse, especially psychostimulants. In addition, neurons in the nucleus accumbens and other limbic areas project to the VTA, providing the substrate for many neurochemicals to modulate the dopamine cells in the VTA.

There are two main experimental paradigms used in animals to assess the effects of drugs and endogenous neurotransmitters, such as dynorphin, on these dopaminergic cells at the level of the VTA. Chemicals can be injected directly into the VTA in order to study their effects. Conditioned place preference is a method that allows the animal to be tested for the reinforcing properties of a chemical in a drug-free state. Also, increases in locomotor activity can be measured, psychomotor stimulants in addition to being rewarding increase locomotor activity, and one substrate underlying this increase is the VTA.

The most extensively studied drugs of abuse, psychostimulants and opiates, both interact with the mesolimbic dopamine system. Future studies fully elucidating the modulation of VTA dopamine neurons will greatly contribute to the understanding of the mechanism of action of drugs of abuse, and may lead to the development of medications to treat drug abusers.

See also **Dopamine; Dynorphin; Limbic System; Neurotransmitters; Nucleus Accumbens.**

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STEPHANIE DALL VECCHIA-ADAMS

VIETNAM ERA STUDY (VES), WASHINGTON UNIVERSITY. Opiates were used extensively by American servicemen deployed to Southeast Asia during the latter part of the Vietnam War. The availability of high-potency heroin increased suddenly in the spring of 1970. Drug-related hospitalizations and deaths among servicemen in Vietnam sharply increased in the following months. A concurrent U.S. drug epidemic accelerated in the late 1960s and continued through the mid-1970s, with heroin use incidence peaking in 1971. The dire prospect of large numbers of returning servicemen addicted to opiates spurred the fear that the heroin epidemic would further spread in the United States.

In June 1971 President Nixon declared the War on Drugs. *Operation Golden Flow*, as facetiously termed by soldiers, commenced at departure locations in Vietnam where soldiers were tested for drugs by urinalysis through the Date Eligible for Return from Overseas (DEROS) program. Soldiers whose urine was positive for narcotics (opiates, amphetamines, or barbiturates) were provided five to seven days of detoxification and treatment prior to their return to the United States. The Special Action Office for Drug Abuse Prevention (SAODAP)—what is now considered the first Drug Czar office—launched a follow-up survey in the United States with the collaboration of the Department of Defense, the Veterans Administration (VA), the National Institute of Mental Health (NIMH), and the Department of Labor. The study was conducted by Washington University School of Medicine in St. Louis, with Lee N. Robins, Ph.D., as principal investigator. The study examined how many men had actually been addicted in Vietnam, and whether those addicted would continue to use heroin or become re-addicted after their return to the United States (Robins, 1974; Robins & Helzer, 1975a).

ORIGINAL STUDY

Two groups of 500 army enlisted men were selected for the first in-person survey, a random sample of veterans returning in September 1971 (general-sample), and another random sample of men whose urines had been positive when tested at DEROS (D+ sample). A total of 898 men were interviewed in 1972 within 12 months of their return from Vietnam. The servicemen were extremely frank: 97 percent of men whose military record showed drug use reported it to the interviewer. Subsequently, a total of 571 veterans were reinterviewed in person in 1974, three years after returning home. A total of 284 nonveterans were also interviewed in 1974 to take into account the natural remission pattern from drug use of men in that age group who were eligible for draft but never served. They were selected from Selective Service registrations and individually matched to the general-sample veterans with respect to draft eligibility, draft board location, age, and education completed by the time of the veteran's entry into service (Robins & Helzer, 1975a).

FOLLOW-UP STUDIES

After two decades of hiatus, Washington University began third and fourth surveys (VES-III & IV) in 1994, with Rumi Kato Price, Ph.D., as principal investigator (Price et al., 2001a, 2001b). The surveys were conducted in collaboration with the VA and with funding from the National Institute of Drug Abuse (NIDA) and later funding from NIMH. Of the total 1,226 veterans and nonveterans whose location information was stored from earlier surveys, 10.5 percent died by the end of 1996, when they would have been 47.5 years old on average if they had been alive (Price et al., 2001b, p. 311). The location rate was more than 93 percent for the surviving members, and 841 men were reinterviewed in 1996–1997. The main purpose of the third study, a 25-year follow-up, was to examine long-term mortality and morbidity consequences of the Vietnam War and drug abuse in middle age. The fourth follow-up, completed in 2006, focused on coping with mental health consequences of war experiences, such as post-traumatic stress disorder (PTSD) and suicidality.

The findings from the earlier 1972 and 1974 follow-ups surprised the scientific community. First, opiate use in Vietnam was much more common than the military had estimated: Almost half (43%) of the army enlisted men had used heroin or opium in Vietnam. Second, 20 percent of the general sample reported being addicted to narcotics (mostly opiates) in Vietnam, but only 12 percent of those addicted in Vietnam became re-addicted in the year after return (Robins et al., 1975b, pp. 957–959). Follow-up interviews two years later showed that this low rate of readdiction

continued. During their second and third years home, addiction rates among drafted men were not significantly greater than among men who qualified for the draft but did not serve. Those who relapsed to narcotics were predominantly men who had used drugs before they entered the service (Robins & Helzer, 1975a). Noteworthy are other reports of this study group and other veterans, which show an excess of alcohol abuse (O'Brien et al., 1980) and poor social adjustment among those with a history of opiate use in Vietnam, as well as the appearance of depressive syndrome associated with combat experience (Helzer et al., 1976).

The third follow-up in 1996–1997 showed that the 25-year cumulative mortality rate since 1971 was 17.4 percent among drug-positive (D+) veterans and 7.4 percent among the remaining general-sample veterans; the nonveteran sample experienced a 2.8 percent mortality rate (Price et al., 2001b, pp. 311–313). Both in-Vietnam and post-Vietnam drug use factors were large and significant independent predictors of mortality, controlling for preservice drug use, continuity to later drug use, and demographic and other behavioral measures (Price et al., 2001b). Among the surviving members, the study found relatively stable patterns of frequent use of sedatives, stimulants, marijuana, cocaine, and opiates over the 25-year period. New relapse to opiates was extremely rare. The mean duration from initiation to the last remission ranged from 9 to 14 years. A majority intentionally attempted to quit illicit drugs; however, most did not use traditional drug treatment in their last attempts. Continued drug dependence often occurred with psychiatric disorders. Whereas 17.2 percent met the criteria for a drug dependence diagnosis since 1972, 20.7 percent met criteria for a lifetime post-traumatic stress disorder (PTSD) diagnosis, according to the *Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition* (*DSM-IV*). The drug dependence rate decreased over time from 45.1 percent in 1971 to 5.9 percent in 1996; on the other hand, PTSD was stable and chronic. The rate of suicidality increased until around 1985, then hovered between seven to eight percent each year after that. Drug dependence increased the likelihood of having PTSD and suicidality during young adulthood. In later years those who were suffering from PTSD or suicidality may have used illicit drugs in part to self-medicate psychiatric symptoms (Price et al., 2004).

Less than nine percent of the then-current drug users in 1996 had been treated for their drug problems in a hospital setting during the previous five-year period. This rate was considerably lower than alcohol abuse treatment and psychiatric treatment among those with PTSD. A selected sample of veterans answered open-ended questions about their health care problems at the fourth follow-up (VES-IV) when they reached their mid-50s. The group at higher risk of suicidality in mid-life was significantly more likely to report both individually-based (such as belief in self-healing and not wanting care) and system-based (such as lack of insurance and bad experience) barriers to care and also more likely to experience negative effects of seeking care (Price et al., 2001a; Virgo et al., 2007). Thirty years after Vietnam, veterans' health care needs still appeared undermet.

See also **Addiction: Concepts and Definitions; Drug Testing Methods and Clinical Interpretations of Test Results; Opioid Dependence: Course of the Disorder Over Time; Vietnam War: Drug Use in U.S. Military.**

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VIETNAM WAR: DRUG USE IN U.S. MILITARY. In the spring of 1971, two members of Congress (John Murphy and Robert Steele) released an alarming report alleging that 15 percent of U.S. servicemen in Vietnam were addicted to heroin. The armed forces were attempting to cope with the drug problem by combining military discipline with "amnesty." Anyone found using or possessing illicit drugs was subject to court martial and dishonorable discharge from the service; but drug users who voluntarily sought help might be offered "amnesty" and brief treatment. This policy apparently was having little impact, as heroin use had increased dramatically over the preceding year and a half.

Because the United States was trying to negotiate settlement of the war, military forces in Vietnam were being rapidly reduced. About 1,000 men were being sent back to the United States each day, many of them to be discharged shortly thereafter to civilian life. If the reported rate of heroin addiction among servicemen were accurate, this rapid reduction in force meant that hundreds of active heroin addicts were being sent home each week. Concerned about the social problems that could ensue from such an influx of addicts, President Richard M. Nixon charged his staff with seeking an effective response. Domestic Council staff members Jeffrey Donfeld and Egil Krogh, Jr., sought advice from Dr. Jerome H. Jaffe, then on the faculty of the University of Chicago, who had previously prepared a report for the president on the development of a national strategy for the treatment of drug dependence. Dr. Jaffe recommended a radical change in the policy for responding to the problem of drug use in the military. The suggested plan included urine testing, to detect heroin use, and treatment rather than court martial when drug use was detected. President Nixon endorsed the plan and the military responded with such remarkable rapidity that, on June 17, 1971, less than six weeks from the time it was proposed, the plan was initiated in Vietnam.

In fact, there was no way to know whether the new approach would be better than the old one, no reliable information on the actual extent of drug use and addiction, and no solid information on which to base estimates of how many servicemen would require additional treatment after discharge. To obtain information on the extent of drug use, the effectiveness of treatment, and the relapse rates it would be necessary to find and interview the servicemen at time of discharge and at various intervals after discharge.

In June 1971, President Nixon also announced the formation of the Special Action Office for Drug Abuse Prevention (SAODAP) charged with coordinating the many facets of the growing drug problem and named Dr. Jaffe as its first director. One of the first tasks of the office was to evaluate the results of the new drug policy for the military, especially as it was implemented in Vietnam. SAODAP arranged for Dr. Lee Robins, of Washington University in St. Louis, to obtain records from the Department of Defense and the Veterans Administration to conduct the study. The findings on drug use prior to and during service are summarized here.

Around 1970, before going overseas, about half the army's enlisted men had had some experience with illicit drugs. However, only 30 percent had tried any drug other than marijuana. At that time, the most common civilian drugs other than marijuana were barbiturates and amphetamines. Before going to Vietnam, only 11 percent of soldiers had tried an opiate, and those who did so generally took cough syrups containing codeine, not heroin or opium.

The men sent to Vietnam had either been drafted or had enlisted. Toward the end of the war, when drug use in the United States was highest, draftees were chosen by a lottery designed to make selection less susceptible to social-class biases. This produced draftees who were a reasonably

representative sample of young American men. Those who enlisted voluntarily, however, who made up about 40 percent of the armed forces, were disproportionately school dropouts. Many of them enlisted before reaching draftable age because of their limited occupational opportunities. They also arrived in Vietnam with considerably more drug experience than the draftees.

Men who were sent to Vietnam before 1969 found marijuana plentiful but little else in the way of illicit drugs (Stanton, 1976). Some amphetamines were available—in part, because the military issued them to help men stay alert on reconnaissance missions. In 1969, heroin and opium began to arrive on the scene, and by 1970–1971 these opiates were very widely available. Marijuana was still the most commonly used illicit drug, but opiates outstripped amphetamines and barbiturates in availability. Heroin and opium were relatively cheap and very pure, so pure that the soldiers could get ample effect by smoking heroin in combination with tobacco or marijuana. This made opiates appealing to men who would have been reluctant to inject them.

At the height of the use of opiates, in 1971, almost half the army's enlisted men had tried them; of those who tried them, about half used enough to develop the hallmarks of addiction—tolerance and withdrawal symptoms (Robins et al., 1975). Marijuana use was even more common; about two-thirds of these soldiers used it. The estimates come from an independent survey of a random sample of army enlisted men eight to twelve months after their return from Vietnam, after the great majority had been discharged (Robins et al., 1975). Previous studies in Vietnam (Stanton, 1972; Roffman & Sapol, 1970; Char, 1972) or among men still in service after return (Rohrbaugh et al., 1974) were less reliable, because of difficulties in collecting a random sample, use of questionnaires rather than interviews (which can lead to careless responses or failure to answer completely), and because the surveys were being done by the army itself, while the men were still subject to possible disciplinary action.

The standard tour of duty for Vietnam soldiers was twelve months. Drug use typically began soon after arrival in Vietnam, showing that it was not at all difficult to find a supplier. Older men used less than younger soldiers, career soldiers less than those serving their first term. Drug experience before induction was a powerful predictor of use in Vietnam (Robins et al., 1980). Essentially all those with drug experience before enlistment used drugs in Vietnam. Of course, there were also some soldiers who used drugs there for the first time.

One interesting observation was that men who drank alcohol in Vietnam tended not to use opiates, and opiate users tended not to drink (Wish et al., 1979). This is a very different pattern from the one seen in the same men both before and after Vietnam, when drinkers were much more likely to use illicit drugs than abstainers.

Soldiers who used drugs had more disciplinary problems, on average, than those who abstained. However, the great majority of drug users received little or no disciplinary action and were honorably discharged. Although there were instances in which drug use impaired a soldier's combat readiness, evidence is lacking that it had much impact on soldiers' ability to carry out orders or wage war.

See also **Addiction: Concepts and Definitions; Drug Testing Methods and Clinical Interpretations of Test Results; Military, Drug and Alcohol Abuse in the United States.**

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LEE N. ROBINS

VIOLENCE AND DRUGS. *See* Aggression and Drugs: Research Issues.

VITAMINS.

Vitamins are organic substances that are required in small amounts for normal functioning of the body. Lack of adequate quantities of vitamins results in well-known deficiency diseases, such as scurvy from Vitamin C deficiency and rickets from Vitamin D deficiency in childhood. For the most part, vitamins are not synthesized by the body but are found in a variety of foods, hence the need for a well-balanced diet or supplementation by taking the vitamins separately.

In the United States, daily minimum requirements for vitamins are recommended and periodically reassessed by the Food and Nutrition Board of the National Academy of Science, National Research Council. Some professionals advocate taking larger amounts of certain vitamins is for better health or for disease prevention or therapy. The question of whether vitamins are drugs is, in one sense, a semantic issue. Sometimes very high doses of a vitamin can actually be used as a medication. For example, in very high doses—twenty or more times higher than needed to prevent the vitamin deficiency disease pellagra—niacin, a member of the B vitamin complex, lowers blood levels of cholesterol and triglycerides, and niacin is commonly prescribed for this purpose.

It is possible to overdose and have serious side effects from large quantities of certain vitamins, such as Vitamins A and D. Therefore, taking larger than needed amounts of vitamins should be done only with the advice of a physician. Deficiencies in vitamin intake can occur under a variety of situations including poverty, dieting, or certain disease states where antibiotics or other factors reduce vitamin absorption. Individuals who drink large quantities of alcohol, for example, without adequate attention to diet often become deficient in some vitamins, such as B_1 (thiamine), and may require their administration to avoid serious and permanent toxicity. Prolonged serious shortages of Vitamin B_1 can cause the death of certain neurons in the brain, a situation that leads to confusion and severe impairment of short-term memory (Wernicke-Korsakoff syndrome).

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MICHAEL J. KUHAR

VULNERABILITY AS A CAUSE OF SUBSTANCE ABUSE. *See* Risk Factors for Substance Use, Abuse, and Dependence.

WASHINGTON UNIVERSITY VIETNAM ERA STUDY (VES). *See* **Vietnam Era Study (VES), Washington University.**

WELFARE POLICY AND SUBSTANCE ABUSE IN THE UNITED STATES. Typical of income maintenance schemes in liberal welfare states, the U.S. system emphasizes economic returns to work. Thus, the U.S. income maintenance system is divided into two tracks, based on the relationship of beneficiaries to the labor force. For the insurance-like programs, notably Old Age and Survivors Insurance (what Americans refer to colloquially as *Social Security*), Social Security Disability Insurance, and Unemployment Compensation; eligibility is linked to an applicant's history of payroll deductions—contributions from wages to the public fund that supports the program. The welfare programs, on the other hand, are means-tested. That is, eligibility depends on meeting strict limits on current earnings and accumulated wealth. Welfare programs are for very poor people, and benefits are substantially less than those paid by the insurance-like programs.

The U.S. system is categorical. For the most part, eligibility is based on membership in a particular category defined by administrative rules: Old age benefits are for those who meet the administrative definition of aged status; disability benefits are for those who meet the medical and vocational standards defining that category, and so forth. Except as discussed below in connection with General Assistance, there are no welfare programs for healthy, non-elderly adults without children.

Finally, the income maintenance system in the United States is funded and administered by federal, state, and local (primarily county) governments. Insurance-like programs are usually funded and administered by the federal government, thus creating a significant degree of uniformity in benefits and eligibility rules. Welfare programs, however, usually are funded and administered by two or more levels of government, so benefit levels and eligibility rules vary considerably among political jurisdictions.

This entry concerns the intersection of substance abuse and initial and continuing eligibility for welfare programs in the context of important policy changes made during the 1990s. It focuses on Temporary Assistance for Needy Families (TANF); Supplemental Security Income (SSI), a federally funded and administered welfare program for the elderly, blind, and disabled; and, to a lesser extent, General Assistance (GA), a state and local form of assistance.

TEMPORARY ASSISTANCE FOR NEEDY FAMILIES

For 60 years after enactment of the Social Security Act of 1935, the United States' cash assistance program for impoverished families was Aid to Families with Dependent Children (AFDC; Aid to Dependent Children until 1961). As the result of

liberal court rulings in the 1960s and the separation of casework from the financial administration of recipients' grants in 1972, AFDC became substantially free of the restraints that characterized an earlier era when social workers raided the houses of welfare mothers to search closets for evidence of a man in the house, who might be made to support the women and their children. Although various work incentives were tried over the years, particularly during the 1980s, they had indifferent results and affected relatively few recipients. Even so, only a small percentage of AFDC families remained on the rolls for years at a time, and most AFDC heads of household, the great majority of them women between 18 and 35 years old, worked part-time or intermittently while raising their children.

However, the ascendancy of the Republican Party following the November 1994 elections yielded the Personal Responsibility and Work Opportunity Reconciliation Act (PRWORA) of 1996 (P.L. 104–193). The PRWORA was based on premises laid out succinctly in *Contract with America*, the 1994 campaign manifesto drafted by Republican leaders in the House of Representatives. *Contract* opined that the liberal welfare regime dating from the 1960s "had the unintended consequence of making welfare more attractive than work" (p. 67). Moreover: "Government programs designed to give a helping hand to the neediest of Americans have instead bred illegitimacy, crime, illiteracy, and more poverty." Welfare reform should thus "change this destructive social behavior by requiring welfare recipients to take personal responsibility for decisions they make" (p. 65).

Reauthorized in 2006, the PRWORA's countermeasures are a complicated combination of incentives and punishments directed at both welfare recipients and the states. The act creates a lifetime limit of 5 years of welfare receipt for TANF families. Further, its funding mechanism requires that each year the states move progressively greater numbers of TANF parents into jobs or face cuts in the overall federal grant to the state (known as a *block grant*). Each state may exempt a small percentage of its caseload from job placement, but in the long run the states are faced with the formidable task of making work-ready and placing in employment thousands of mothers with little work experience and few marketable skills. At the same time, the PRWORA permits the states a great deal of flexibility in using various funds to create training programs, support childcare, and even fund alcohol and other drug treatment.

The PRWORA also requires or permits the states to enforce a variety of behavioral requirements for continuing eligibility for full TANF benefits. Among these, the PRWORA permits states to mandate treatment for alcohol and other drug abusers as well as to require random drug testing under the threat of forfeited benefits. (A failed provision of the original legislation would have forced the states to implement these provisions.) Research on TANF parents has found that the prevalence of substance-use disorder in the adult TANF population, as measured by a rigorous standard, is very similar to that in the population at large: about 8 to 10 percent. Except in connection with the drug felon ban discussed below, few states have expressed serious interest in drug testing or mechanisms for mandatory treatment that are not triggered by new criminal behavior or the abuse or neglect of children. In these cases, the mandate for treatment arises outside of the welfare system itself.

A further drug-related provision of the PRWORA is both more stringent and more common. The act provides that unless a state passes contrary legislation, any person with a felony drug conviction after August 22, 1996 (the date PRWORA was signed into law), will be banned for life from TANF (among other federal benefits). This provision reflected a negotiated compromise on the House of Representatives version of the act that would have extended the ban to those convicted of misdemeanors. The drug ban has proved extremely unpopular in the states. By 2006, 32 states had opted out of the ban or dramatically modified it, and others were in the process of doing so. One modification applied in a few states is a requirement for treatment and sometimes subsequent urine testing of TANF-eligible drug felons.

SUPPLEMENTAL SECURITY INCOME

Since 1950 the federal government has provided income support from welfare or social insurance to individuals with work disabilities unrelated to military service. In 1972 welfare programs for the disabled, blind, and impoverished elderly that had been administered and funded in collaboration

with the states came under the federal administration and financial support of Supplemental Security Income (SSI).

From the first SSI payments in January 1974 until March 1996, drug addiction and alcoholism (DA&A) were treated as potentially disabling impairments, but until about 1990 relatively few applicants qualified on this basis. Indeed, there were fewer than 10,000 DA&A cases on SSI as late as the end of 1986. By mid-1996, however, there were almost 166,000. Most of this growth seems to have resulted from four factors. First, federal circuit court decisions during the mid-1980s removed substantial technical obstacles to claimants seeking benefits on the grounds of addiction. Second, in the wake of these decisions many state and county governments set out to transfer recipients of General Assistance, a welfare program supported entirely with state and local funds, to SSI (a federally-funded program). To promote this process, some states or counties contracted with private non-profit legal advocates to support applications and appeals. When the DA&A SSI population is disaggregated by state, it is clear that California, Michigan, Illinois, and a few others made much higher per capita use of the DA&A category than did other states. For example, by 1996 Oregon had as many DA&As on SSI as Texas, a state with several times the adult population of Oregon.

The last two contributors to the growth in the DA&A rolls are related to a famous Reagan-era controversy concerning Social Security disability programs. During the early 1980s, responding in part to a Carter administration initiative and also drawing on a similar tactic applied during his governorship of California between 1967 and 1974, President Reagan's Social Security administrators launched a roll-cutting campaign that relied on continuing disability reviews (CDRs). As a result, more than 500,000 people lost federal disability benefits, a large percentage of them people with mental illness. Subsequent backlash from the courts and Congress restored many to the rolls, further liberalized eligibility criteria, and all but paralyzed the CDR process for years to come. As a result of perennially backlogged CDRs, many DA&As who regained their ability to work remained on the rolls, particularly as the economic conditions of the late 1980s and early 1990s provided few opportunities for poor, unskilled, ill-educated people. In part as the result of this episode and in part due to the dramatic rise in homelessness during the 1980s, the Social Security Administration was charged with increasing its outreach efforts, especially among homeless people. This brought more DA&As into the application process.

Throughout the history of SSI, the Social Security Administration saw the operation of its program for DA&A cases as low-priority. With no specific appropriations from Congress to ensure that DA&As received treatment or were separated from the rolls for failing to participate and with no resources to thoroughly investigate the relationship of beneficiaries to representative payees (those who receive their checks and supervise their expenditures), the agency allowed the program to drift. However, it attracted a great deal of critical and unwanted attention as it grew rapidly. Beginning in 1991, the program was the subject of unflattering reports from federal watchdog agencies and a mounting number of highly publicized incidents involving DA&A recipients using benefits to purchase drugs and signing up representative payees (like bartenders) with little fiduciary interest in them. The more scandalous claims about the program were largely unfounded, but many legislators and representatives of the alcohol and drug treatment community saw the DA&A program as enabling addiction. Moreover, the program's rapid growth, and the Social Security Administration's apparent inability to curb it, lent credence to the claim that it was an entitlement program "out of control" in an era of bipartisan fiscal retrenchment.

In August 1994, after Congressional hearings and national media coverage (almost exclusively negative), Congress limited DA&A benefits to three years and reiterated the necessity to participate in treatment. Although the Social Security Administration made no effort to defend the DA&A program, it worked very hard to implement treatment referral and monitoring arrangements in all of the states. But as it did so, the November 1994 elections shifted control of the House of Representatives to conservative Republicans who were against the program.

On March 29, 1996, Congress eliminated the DA&A category in SSI and Social Security Disability Insurance (DI), the first time any qualifying impairment had been legislated out of existence.

The benefits of 209,000 recipients of SSI and DI ceased after 1996 unless they applied for redetermination and were reclassified based on other impairments (mental illness, for example). Only 34 percent were restored to the rolls.

In retrospect, the demise of the DA&A program seems to have been over-determined. It was at once culturally problematic and, thus deprived of a unified constituency, extremely difficult to administer (and thus disliked by the Social Security Administration). As a result of its administrative problems, the program was susceptible to discrediting. The program left behind a legacy of mandatory treatment and representative payee provisions that seem to have become more common features of state and local welfare reform measures, but no observers see any chance of its resurrection at the federal level in the foreseeable future.

GENERAL ASSISTANCE

General Assistance (known in some places as General Relief) is a form of welfare financed and operated entirely by state, county, or municipal governments. Many states do not have GA programs, or GA exists only in some local jurisdictions. GA benefit levels and eligibility rules also vary from state to state, and in some states, notably California and Wisconsin, from county to county. Some states (or smaller jurisdictions) provide GA benefits merely on the basis of need, but most GA programs are categorical (e.g., Oregon and Washington), restricting eligibility to older people not yet eligible for Social Security or Supplemental Security Income (SSI), to parents waiting for TANF benefits or temporarily suspended from that program, to those with an SSI application pending, or to those who are realistically unemployable by some criteria of age and infirmity, but who do not meet the stringent disability criteria of SSI. GA programs also vary in the way that benefits are paid: by cash, by rent and food vouchers, or some combination. Some GA programs are time-limited (in Pennsylvania, e.g.). All GA programs have extremely low benefits in the range of $200–$250 per month.

Probably due to the overrepresentation of single men among GA beneficiaries, many jurisdictions estimate that the prevalence of alcohol and drug problems among GA recipients is several times that of the general population. Historically, GA has been the welfare program most accessible to people with alcohol and other drug problems. After World War II, many large cities used some combination of cash, hotel vouchers, and restaurant chits to keep single, addicted men (mainly) housed and fed without giving them much money to handle. This system was largely abandoned as the cost of its administration rose. However, with the elimination of addiction as a qualifying impairment in the SSI program, some cities and counties have revived such arrangements. In San Francisco this system is called "Care Not Cash."

CONCLUSION

The thrust of recent federal welfare reform has been to rely on fiscal incentives and penalties to encourage welfare recipients to work and state governments to see that they do. As a corollary, welfare eligibility is once again being used as leverage on the behavior of poor people, and drinking and drug use have been salient targets of this effort—whose complete effects remain to be seen. Given the resources (no small caveat), many state and local General Assistance programs seem inclined to follow suit.

See also **Economic Costs of Alcohol and Drug Abuse; Funding and Service Delivery of Treatment; Homelessness, History of Association with Alcohol and Drugs.**

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JIM BAUMOHL

WIKLER'S CONDITIONING THEORY OF DRUG ADDICTION. Abraham Wikler (1910–1980) was one of the founding researchers of the United States Public Health Service Addiction Research Center, in Lexington, Kentucky. (It is now the Intramural Program of the National Institute on Drug Abuse in Baltimore, Maryland.) Wikler, a psychiatrist, was particularly interested in understanding why the heroin addicts he interviewed at Lexington so frequently relapsed after treatment, long after any signs of acute opiate withdrawal had subsided. He was intrigued by their reports that upon returning to their old neighborhoods, they felt as if they were experiencing withdrawal symptoms. In 1948 he began to develop his theory about the role of conditioning in addiction, and over the next 30 years he continued to elaborate on this theory and its implications for understanding and treating addictions.

Within Wikler's model, opioids such as heroin or morphine are viewed as having pharmacological effects that reduce certain *needs,* thereby reinforcing the behavior that leads to their repeated use (operant reinforcement). He proposed that the behavioral chain leading to addiction often begins when a young person with prevailing moods of hypophoria (feeling unliked or unappreciated) and anxiety, frequently combined with a strong need to belong to some identifiable group, uses heroin in response to peer pressure. The drug reduces hypophoria and anxiety, and the drug-using behavior is reinforced both by those effects and by increased peer group acceptance. With repeated drug use, especially of opioids, tolerance and physical dependence develop.

Wikler recognized that the small degree of physical dependence that develops after only a few doses of an opioid drug, and the aversive quality of withdrawal, create a new *need state*, the need to alleviate the withdrawal syndrome. For short-acting opioids such as heroin, withdrawal begins a few hours after the last dose, so the user self-administers the drug several times a day. Because a heroin user who is physically dependent frequently experiences some degree of withdrawal between doses, recurring environmental stimuli (street associates, neighborhood surroundings, drug paraphernalia, drug dealers) prompt feelings of withdrawal, which become classically conditioned to these stimuli. Furthermore, internal stimuli—such as anxiety, stress, or depression—that are experienced when withdrawal occurs may also become linked to withdrawal, and these emotional states can trigger conditioned withdrawal and craving in former addicts who have been free from drugs for many months. If someone who was formerly addicted responds to the conditioned withdrawal by using drugs, the cycle is initiated anew.

Even in his earliest writings Wikler noted that the acute opioid withdrawal syndrome, which typically lasts for one to four weeks, is followed by a more protracted state of physiological abnormality that often lasts several months; and during this period the impact of conditioned withdrawal and associated craving may be of considerable importance in leading to relapse. Subsequent work by William Martin and colleagues clearly demonstrated the existence of such a protracted opioid withdrawal syndrome.

Wikler also saw a role for the *hustling* behavior required to obtain illicit drugs (earning or stealing enough to get drugs, seeking *connections*, *scoring*, and avoiding arrest). Hustling is at first maintained by getting and using heroin; but with time, Wikler postulated, it becomes a self-reinforcing behavior as a result of the sense of achievement felt for having successfully survived another day on the street.

Wikler argued that conditioned responses did not simply decay with the passage of time, but required some form of active extinction. Thus, the practice of treating addicts in a drug-free environment, even for several months, left them vulnerable to relapse when they returned to an environment where drugs were available. The former stresses were likely to occur again, and the previous drug use had become conditioned to external and emotional stimuli. Wikler proposed that one way to extinguish the linkage between operantly reinforced drug use and conditioned withdrawal would be for the addict to engage in the usual rituals of working to get and use drugs but to experience no reinforcement from the drug's actions. He suggested that the use of long-acting opioid antagonist drugs such as cyclazocine and naltrexone, developed by Martin and colleagues in the late 1960s, might permit a test of this approach.

Subsequent research found that even when opioid addicts volunteered to take these antagonists, they were rarely willing to continue taking them, and so antagonist treatment did little to alter the likelihood of relapse. Martin suggested that because opioid antagonists did not alleviate hypophoria, the addicts' lack of enthusiasm for them was understandable. But since the development and approval, in the early twenty-first century, of long-acting (depot) forms of naltrexone that make compliance with taking the drug less problematic, new efforts are underway to determine if such opioid antagonists can play the useful role in the treatment of opioid addiction that Wikler foresaw for them.

Wikler's ideas about the operant reinforcement of drug-taking and development of conditioned withdrawal in response to external and emotional stimuli are generally accepted by most experts in the field of addiction treatment. However, very few programs attempt to treat addictions by seeking to extinguish the learned behavior by means of extinction. For example, although the theoretical concepts underlying the present-day widespread use of relapse prevention and cognitive-behavioral therapy (CBT) seem at first to be closely related to Wikler's ideas about the role of learning and conditioning, this treatment approach emerged from different clinical observations and led to very different treatment procedures. Like Wikler, the developers of CBT emphasized the role of learning—both operant and classical (conditioned)—in the genesis of addiction, but combined this understanding with cognitive psychology, behavior modification, social skills training, and efforts to help patients recognize that a single episode of alcohol or drug intake need not lead to a full relapse. Rather than aiming for extinction of drug use, CBT tries to teach the patient how to avoid the situations and emotions that are likely to trigger a relapse and to develop nondrug techniques for controlling aversive emotional states (coping skills).

Because of his own observations of addicts maintained on opiates, Wikler was skeptical about the theory underlying Vincent Dole's and Marie Nyswander's work with methadone. Dole and Nyswander saw opiate addiction as a persistent metabolic disorder (*drug hunger*) induced by opiate use. They argued that this drug hunger could be corrected by maintaining addicts on appropriate doses of methadone which, they believed, would allow former addicts to be essentially normal and to exhibit little or no psychopathology. Like Dole and Nyswander, Wikler recognized that protracted withdrawal and its associated craving could contribute to relapse, but he did not assign it so central a role in relapse. Wikler's perspective was that whatever form of psychopathology may have contributed to the initial use of a drug, the repeated reinforcement of the drug-using behavior, and the linkage of withdrawal symptoms through conditioning to environmental stimuli and to internal states such as anxiety and stress created a new disorder—a disease *sui generis*.

In short, Wikler, as well as Dole and Nyswander, viewed opioid addiction not as a character defect or hedonistic pursuit of euphoria, but as a distinct disorder that arose as a result of repeated use of opioid drugs.

See also **Opioid Complications and Withdrawal; Treatment, Behavioral Approaches to: Cognitive-Behavioral Therapy.**

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JEROME H. JAFFE

WITHDRAWAL

This entry includes the following essays:

ALCOHOL

The human nervous system undergoes an adaptation in response to the chronic consumption of alcohol (ethanol). If the consumption is heavy enough (adequate dose) and occurs for a long enough time period (adequate duration), a rapid decrease or sudden cessation of drinking will result in a withdrawal syndrome. This syndrome occurs in association with re-adaptation of the nervous system to a drug-free state. The dose and duration of alcohol consumption required to produce a withdrawal syndrome in a given population, or even a given individual, are difficult to predict, because no well-controlled studies have been conducted (or are likely to be, for ethical reasons). Such studies have been done in animals, however.

In the nondrinker or social drinker who consumes alcohol to the point of intoxication, symptoms of a "hangover" (e.g., insomnia, headache, and nausea) may ensue. It has been suggested that these are symptoms of acute alcohol withdrawal, but that interpretation is controversial, and other explanations (e.g., dehydration) have also been proposed to explain hangover symptoms. Usually, no treatment is required, and there are no serious consequences from a hangover.

ALCOHOL DEPENDENCE AND WITHDRAWAL

The natural progression of alcohol dependence leading to the point of requiring detoxification usually takes 15 to 20 years. The average age of persons admitted to detoxification units in the United States is around 42 years, although detoxification services may be required at almost any age. The withdrawal syndrome seen in persons requiring detoxification ranges from a mild degree of discomfort to a potentially life-threatening disorder.

The severity of the withdrawal syndrome is dependent on both the dose and duration of alcohol exposure. In studies conducted on rats, a severe withdrawal syndrome has been seen following high-level exposure to alcohol in a vapor chamber in as short as a week. The administration of alcohol directly into the rat's stomach is associated with a longer time period for the acquisition of physical dependence. In humans, the severity of withdrawal depends also on the amount of alcohol consumed and the time period over which it has been consumed. For practical purposes, this can be measured in terms of the amount ingested on a daily basis for the weeks and months preceding detoxification. One study of inpatients (federal prisoners and narcotic users) demonstrated that the consumption of 442 grams of alcohol, or 32 standard drinks per day for about two months (a standard drink being 13.6 grams, or 0.6 fluid ounces, of alcohol, the amount in 12 oz. of beer, 5 oz. of wine, or 1.5 oz. of liquor) results in a major withdrawal syndrome in all subjects, whereas the consumption of 280 to 377 grams (21 to 28 standard drinks) per day results in a mild syndrome of anxiety and tremor (Isbell et al., 1955).

Studies that involve patients (as opposed to research subjects) have not been able to demonstrate a consistent relationship between recent alcohol consumption and the severity of the withdrawal syndrome (Shaw et al., 1981). This in part relates to the lack of accurate recall of exact quantities consumed within a given time period. Furthermore, in the real world there are different patterns of consumption (e.g., some drinkers consume alcohol in a binge pattern, whereas others drink in a more regular pattern), and different drinkers have varying durations of lifetime exposure to alcohol. One drinker may take two or three years to become dependent, another may take 15 years, and yet another 40 years. In addition, a person who has previously experienced significant alcohol withdrawal may be at higher risk for developing a repeat withdrawal, both in terms of the severity of the syndrome and the rate of reacquisition of physical

dependence. In these individuals, it takes a shorter time to become re-addicted, a situation that has been attributed to sensitization (or "kindling") of the central nervous system (Bayard et al., 2004). Other factors that may be implicated in the severity of the withdrawal syndrome include age, nutritional status, and the presence of concurrent physical disorders or illness such as pancreatitis or pneumonia (Sullivan & Sellers, 1986). Alcoholics are at increased risk for these and other medical disorders.

WITHDRAWAL SYMPTOMS

The symptoms of alcohol withdrawal appear in inverse relation to the elimination of alcohol from the body, which can be measured via the blood alcohol concentration (BAC). Many alcoholics note this phenomenon on a daily basis; that is, they require a drink in the morning to suppress tremor and anxiety, or to "steady the nerves." Some of the more common symptoms of alcohol withdrawal are: anxiety, agitation, restlessness, insomnia, a "shaky" feeling, anorexia (loss of appetite), nausea, changes in sensory perception (e.g., itchy skin, sounds seem louder, lights look brighter), headache, and palpitations. These are often accompanied by vomiting, sweating, an increased heart rate, an increase in blood pressure, tremor (shakiness of hands, and sometimes of the face, eyelids, and tongue), and seizures.

More severe withdrawal is associated with an intensification of the above symptoms and signs, together with a progression to tactile, auditory, and visual hallucinations (e.g., feeling, hearing, and seeing things that are not there), disorientation, and confusion (delirium tremens, or the "DTs") (Bayard et al., 2004). After stopping alcohol consumption, the more common and milder symptoms usually reach a peak after 12 to 24 hours, and they have mostly subsided by 48 hours after consumption has ceased (Sellers & Kalant, 1976). More severe, or late, withdrawal symptoms usually reach a peak at around 72 to 96 hours, and these are potentially life threatening. Less than 5 percent of persons withdrawing from alcohol (depending on how they are selected) are estimated to develop a severe reaction. With appropriate drug treatment, an even lower percentage is estimated to develop a major withdrawal reaction. Under ideal circumstances, there should be almost no mortality from this disorder on its own, so overall mortality ought to be similar to that of any concurrent medical disorder.

An assessment of the severity of withdrawal can be accomplished on the basis of clinical experience or with the assistance of various rating instruments. One of the simplest and easiest to administer is the Clinical Institute Withdrawal Assessment for Alcohol, Revised (CIWA-Ar). This assessment tool consists of 10 items that can be scored at frequent intervals, and a health-care provider can administer it in less than a minute (see Figure 1).

TREATMENT

The goals of treatment for alcohol withdrawal syndrome are to relieve discomfort and to prevent complications. Kasser et al. (1997) identify some immediate goals in detoxifying patients of alcohol and other abused substances: (1) "to provide a safe withdrawal from the drug(s) of dependence and enable the patient to become drug-free," (2) "to provide a withdrawal that is humane and thus protects the patient's dignity" and (3) "to prepare the patient for ongoing treatment of his or her dependence on alcohol or other drugs." Treatment consists of supportive care, general drug treatment, and specific drug treatments.

Supportive care consists of reassurance; reality orientation; reduced sensory stimuli (e.g., a dark, quiet room); attention to fluid and electrolyte balance, nutrition, physical comforts, and body temperature; sleep and rest; and positive encouragement toward long-term rehabilitation. Most patients can be treated with supportive care alone, but it is impossible to predict which patients will require more intensive care.

General drug treatment includes the B vitamin thiamine, which should be given to all patients to prevent the brain damage that commonly occurs in alcoholics who are thiamine deficient. In varying degrees, thiamine deficiency occurs commonly in alcoholics, and it is thought to result from several factors, including poor diet, malabsorption of the vitamin, excess excretion of the vitamin, and altered metabolism and physiologic trafficking of the vitamin within the body. Thiamine deficiency contributes to neuronal damage and cell death through four main effects caused by changes in intracellular metabolism: (1) a disruption in the production of key molecules required for cell structure and function, such as the myelin sheath on

Addiction Research Foundation Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar)

Patient _____ Date | ___ | ___ | ___ | (y m d) Time _____ : _____ (24-hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute: _____ **Blood pressure:** _____/ _____

NAUSEA AND VOMITING—Ask "Do you feel sick to your stomach? Have you vomited?" Observation.
0 no nausea and no vomiting
1 mild nausea with no vomiting .
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

TREMOR—Arms extended and fingers spread apart. Observation.
0 no tremor
1 not visible, but can be felt fingertip to fingertip
2
3
4 moderate, with patient's arms extended
5
6
7 severe, even with arms not extended

PAROXYSMAL SWEATS—Observation.
0 no sweat visible
1 barely perceptible sweating, palms moist
2
3
4 beads of sweat obvious on forehead
5
6
7 drenching sweats

ANXIETY—Ask "Do you feel nervous?" Observation.
0 no anxiety, at ease
1 mildly anxious
2
3
4 moderately anxious, or guarded, so anxiety is inferred
5
6
7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

AGITATION-Observation.
0 normal activity
1 Somewhat more than normal activity
2
3
4 moderately fidgety and restless
5
6
7 paces back and forth during most of the interview, or constantly thrashes about

VISUAL DISTURBANCES—Ask "Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there? Observation.
0 not present
1 very mild sensitivity
2 mild sensitivity
3 moderate sensitivity
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

TACTILE DISTURBANCES—Ask "Have you any itching. pins and needles sensations, any burning, any numbness or do you feel bugs crawling on or under your skin?" Observation
0 none
1 very mild itching, pins and needles, burning or numbness
2 mild itching, pins and needles, burning or numbness
3 moderate itching, pins and needles, burning or numbness
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

AUDITORY DISTURBANCES—Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
0 not present
1 very mild harshness or ability to frighten
2 mild harshness or ability to frighten
3 moderate harshness or ability to frighten
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

HEADACHE, FULLNESS IN HEAD—Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
0 not present
1 very mild
2 mild
3 moderate
4 moderately severe
5 severe
6 very severe
7 extremely severe

ORIENTATION AND CLOUDING OF SENSORIUM-Ask "What day is this? Where are you? Who am I?"
0 oriented and can do serial additions
1 cannot do serial additions or is uncertain about date
2 disoriented for date by no more than 2 calendar days
3 disoriented for date by more than 2 calendar days
4 disoriented for place and/or person

Total CIWA-A Score _____
Rater's Initials _____
Maximum Possible Score 67
This scale is not copyrighted and may be used freely.

Figure 1. Addiction Research Foundation Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar). ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

neurons; (2) lactate accumulation; (3) glutamate accumulation and subsequent excitotoxicity, overstimulation of neurons by excitatory neurotransmitters leading ultimately to neuronal death; and (4) cellular energy deficits.

The prompt replacement of thiamine (and to some degree the other B vitamins) is essential in preventing and treating the neuronal damage that occurs from its depletion. The most severe form of thiamine deficiency, Wernicke-Korsakoff syndrome, can also be abruptly induced by glucose infusion prior to vitamin replacement in an alcoholic who has low blood sugar. Occasionally, magnesium may be given if there is a severe deficiency and there are potential cardiac problems. Intravenous fluids may be required in uncommon circumstances.

Specific drug treatments may also be given to suppress the signs and symptoms of withdrawal. While more than 100 drug treatments have been suggested for the treatment of alcohol withdrawal, very few adequate scientific studies have been conducted, primarily because appropriate studies are difficult to conduct. In addition, many patients do very well with placebo or supportive care alone. Nevertheless, appropriate and effective specific treatments are available. These consist of drugs belonging to the same general class as alcohol (central nervous system depressants). The drugs of choice are the longer-acting benzodiazepines (usually diazepam [Valium] or chlordiazepoxide [Librium]), but shorter-acting benzodiazepines (such as lorazepam [Ativan], and oxazepam [Serax]) are often used to avoid the cumulative effects of repeated doses.

The specific drug treatment is usually given either before most withdrawal has occurred (substitution or prophylactic treatment) or after significant symptoms and signs manifest themselves (suppressive treatment). The advantages of substitution treatment include the prevention of discomfort and the more severe withdrawal symptoms. The disadvantages include unnecessary treatment for some patients. The advantages of suppression treatment include more appropriate titration, or determination, of the dose of medication for a given patient's needs. The disadvantages include unnecessary patient discomfort, at least initially; the potential for development of more severe withdrawal; and drug-seeking behavior by patients. Benzodiazepines have been demonstrated to prevent complications of serious withdrawal, such as seizures, hallucinations, and cardiac arrhythmias (Sellers et al., 1983). In general, high doses of these benzodiazepines (with medium-to-long half-lives) are provided early in treatment to cover the patient for the time period of acute withdrawal (usually between 24 to 48 hours after cessation of alcohol consumption). Rarely do patients require very large doses of these drugs (e.g., several hundred milligrams of diazepam) to suppress symptoms and signs. Patients with histories of withdrawal seizures (convulsions), or those that have epilepsy, are always treated prophylactically, usually with benzodiazepines and any other anticonvulsant medication that they are prescribed on a regular basis. Patients who develop hallucinations are often given (in addition to benzodiazepines) haloperidol (Haldol) or another antipsychotic medication. These drugs are effective in the treatment of hallucinations.

Since the late 1990s, there has been some enthusiasm for the use of anticonvulsants as a primary treatment for alcohol withdrawal, and also as adjunctive treatments to the benzodiazepines. These drugs may indeed be effective, particularly in milder cases of withdrawal. Beta-blockers such as atenolol can be used to reduce cardiovascular strain and regulate the heart rate, but caution must be used in this approach because it does not treat the underlying withdrawal syndrome and could mask worsening withdrawal symptoms, thereby preventing adequate treatment with benzodiazepines.

In summary, alcohol withdrawal syndrome is a constellation of symptoms and signs that accompany the detoxification and re-adaptation of the nervous system to a drug-free state in chronic users. In most cases, these signs and symptoms are a source of mild discomfort and run a self-limited course. Occasionally, more severe withdrawal occurs or patients have concurrent complications (e.g., seizures). Under these circumstances appropriate drug treatment is mandatory to relieve symptoms and prevent complications.

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BENZODIAZEPINES

Like many other drugs that alter central nervous system (CNS) neurotransmission, benzodiazepines may produce a withdrawal syndrome when the drugs are abruptly discontinued. These withdrawal symptoms, including increased anxiety and insomnia, are often the mirror image of the therapeutic effects of the drug. Since the term *withdrawal* is usually applied to drugs of abuse, these symptoms are sometimes called *abstinence syndrome* or *discontinuance syndrome* when associated with benzodiazepines when used as prescribed, thereby distinguishing these substances from abused drugs such as alcohol and cocaine or the non-therapeutic use of opioids or barbiturates.

ETIOLOGY

Not all patients who take benzodiazepines experience a discontinuance syndrome when the drug is stopped. Several conditions must be present before the discontinuance syndrome is likely:

Duration of treatment. The benzodiazepine must be taken for long enough to produce alterations in the CNS that predispose individuals to a discontinuance syndrome. When benzodiazepines are taken at a therapeutic dosage, the range of time that usually produces a discontinuance syndrome is from several weeks to several months. Taking benzodiazepines once or twice during a crisis, or even for several weeks during a prolonged period of stress, ordinarily does not set the stage for discontinuance symptoms.

Dose. The amount of drug taken on a daily or nightly basis is also a critical factor. When higher-than-therapeutic doses are taken—for example, for treatment of panic disorder—then the period required before a discontinuance syndrome may develop is shortened.

Abrupt discontinuance of the benzodiazepine. Discontinuance symptoms arise because the level of drug at the CNS receptor sites is suddenly diminished. Since drug level in the CNS is proportional to the amount circulating throughout the body, an abrupt decline in CNS drug levels occurs when the blood level abruptly drops. Gradual tapering of benzodiazepines usually prevents the appearance or reduces the intensity of discontinuance symptoms.

Type of benzodiazepine. Benzodiazepines are classified into short and long half-life compounds (see Table 1). These terms refer to the time it takes for the body to remove (clear) the benzodiazepine. Short half-life benzodiazepines are cleared very rapidly, usually from four to about 16 hours, depending on the drug. In contrast, long half-life

Generic name	U.S.Brand name	Half-life	Commonly used dose range	Duration of therapeutic action	Common therapeutic Indications
Alprazolam	Xanax	11.2 hours	0.5–4.0 mg/day	3–4 hours	Anxiety
Lorazepam	Ativan	12 hours	2–6 mg/day	4–6 hours	Anxiety
Temazepam	Restoril	3.5–18.4 hours	7.5–30 mg/day	4–8 hours	Insomnia
Clonazepam	Klonopin	30–40 hours	0.5–4 mg/day	6–8 hours	Anxiety
Diazepam	Valium	20–54 hours	5–40 mg/day	varies	Anxiety, Insomnia

SOURCE: Adapted from Thomson Micromeded, 2008.

Table 1. Characteristics of different benzodiazepines' withdrawal symptoms. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

benzodiazepines may take anywhere from 24 to 100 or more hours to be cleared. Since the appearance of discontinuance symptoms depends, in part, on the rapidly diminishing blood level of the drug, abrupt cessation of the short half-life benzodiazepines is more likely to produce discontinuance symptoms. Controversy existed as of 2008 about whether other factors that distinguish one benzodiazepine from another are associated with the appearance of a discontinuance syndrome.

MANIFESTATIONS

Virtually all who experience discontinuance symptoms from benzodiazepines describe increased anxiety, restlessness, and difficulty falling asleep. These symptoms may be mild, little more than an annoyance for a few days, or they may be quite severe and even more intense than the symptoms of anxiety or insomnia for which the drugs were initially prescribed. The reappearance of the initial symptom, such as anxiety or insomnia, only in greater severity, is known as a *rebound symptom*. Rebound symptoms usually occur within hours to days of benzodiazepine discontinuance and then gradually fade. In some cases, however, they may be so intense that the patient resumes taking the benzodiazepine to avoid the discontinuance symptoms themselves. Thus, a cycle of benzodiazepine dependence may begin: The patient takes the drug primarily to treat or prevent rebound discontinuance symptoms from appearing, rather than treating an underlying anxiety or sleep disorder.

Benzodiazepines that are given to induce sleep may also be associated with the development of discontinuance symptoms. Rebound insomnia, the most common discontinuance symptom, typically occurs on the first night and sometimes the second night after discontinuance of short half-life benzodiazepines. Rebound insomnia may be so intense during these nights that the patient may be unwilling to risk another sleepless night and so returns to taking the benzodiazepine hypnotic. Rebound insomnia is less common with long half-life benzodiazepines, though this benefit comes with the possible disadvantage of daytime sedation that is more commonly associated with long half-life benzodiazepines.

If untreated, rebound symptoms may sometimes persist for many months. When this situation occurs it is difficult to determine whether the symptoms are still manifestations of discontinuance or are the result of the return of the problems (anxiety, insomnia) for which the drug was originally prescribed. Sometimes new symptoms that did not exist before the patient took the benzodiazepine appear after discontinuance; these are termed *true withdrawal symptoms*, indicating a change in CNS functioning. Usual withdrawal symptoms include headache, anxiety, insomnia, restlessness, depression, irritability, nausea, decreased appetite, gastrointestinal upset, and unsteadiness. Patients may also experience increased sensitivity for sound and smell, difficulty concentrating, and a sense that events are unreal (derealization) or feeling detached from oneself (depersonalization). Unusual withdrawal symptoms include psychosis and seizures.

OCCURRENCE OF SEIZURES

From a medical perspective, the most serious of all discontinuation symptoms is the development of withdrawal seizures. Seizures are generally grand mal in type (tonic-clonic; epileptic) and

may threaten the life of the patient. They tend to occur only when higher-than-therapeutic doses are abruptly discontinued.

Withdrawal seizures almost always occur when the patient has been taking other drugs, such as antidepressants or antipsychotic agents, which can reduce the threshold for seizures, together with a benzodiazepine.

COEXISTING PSYCHOPATHOLOGY

Apparently some people are more predisposed to develop the discontinuation syndrome than others. Those who have been previously dependent on benzodiazepines, alcohol, or other sedative-hypnotic drugs, such as barbiturates, are more likely to experience discontinuance symptoms after the termination of benzodiazepine therapy. It is especially important, therefore, that such patients never stop taking their benzodiazepines abruptly.

TREATMENT

Although a variety of treatments have been proposed for the discontinuance syndrome, the best approach is to prevent its occurrence. Logically, prevention consists of a very gradual tapering of the benzodiazepine dose, with a firm rule never to discontinue these medications abruptly if they have been taken for more than a few weeks on a regular basis.

Even with gradual tapering, however, some patients may continue to experience rebound or withdrawal symptoms that are sufficiently disturbing to require treatment. Drugs that tend to reduce CNS hyperarousal states, such as anticonvulsants, have sometimes been employed to treat benzodiazepine discontinuance, though their effectiveness in this situation had not been well documented as of 2008. Alternatively, benzodiazepine treatment is restarted using a long half-life compound that is then very gradually tapered.

WITHDRAWAL

For the great majority of patients, benzodiazepine discontinuance is a relatively benign and short-lived syndrome; many, if not most, patients have no difficulty. It is generally agreed that the therapeutic benefits of taking benzodiazepines far outweigh any problems with discontinuance when drug treatment is no longer necessary.

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COCAINE

H. W. Maier first mentioned cocaine withdrawal in his 1928 book *Der Kokainismus*, and early descriptions were provided in the 1980s during an epidemic of cocaine use in the United States. These descriptions emphasized subjective states rather than the physiological symptoms typically observed in sedative, alcohol, and opiate withdrawal (Satel et al., 1991; Weddington et al., 1990). The symptoms are listed in the *DSM-IV* diagnostic criteria for cocaine dependence and include depressive symptoms, poor sleep, lack of energy, agitation, and craving for cocaine. The duration of these withdrawal symptoms is typically a few days but might extend for as long as three to four weeks in some patients. Subjects particularly suffer from difficulty with sleeping. An early stage of withdrawal lasting several hours to a day and often called a crash has been described. During this period patients may appear quite agitated, paranoid, and suicidal. This crash appears to be related to sleep deprivation, which complicates the typical effects of stimulants on cognition and is terminated by the patient sleeping for 10 to 15 hours. Benzodiazepines are often given in emergency settings in order to induce this sleep and end this early period of withdrawal symptoms, when they occur.

The evidence for brain abnormalities associated with chronic cocaine dependence and possibly related to withdrawal symptoms includes electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI) abnormalities (Kosten

et al., 2007). More fundamental abnormalities in brain structure (e.g., size to anterior cingulate cortex) and neuronal receptors (e.g., reduced number of dopamine D2 type receptors on caudate neurons) are evident in these patients but are unlikely to be related to the pathophysiology of any acute withdrawal syndrome. Instead, these abnormalities reflect either inherited traits or damage induced by long-term high dose cocaine use, which would not change quickly during the relatively brief period of cocaine withdrawal.

Protracted withdrawal lasting for several months after acute withdrawal has subsided has been considered for many abused substances with the best evidence for alcohol and opiates (Satel et al., 1993). Little data support such phenomena with stimulants such as cocaine. While many patients relapse weeks and months after stopping cocaine and when the symptoms of acute withdrawal are long gone, these relapses are related to complex psychological processes of cue-induced craving, drug priming, and stressful events that have a neurobiology probably related to general aspects of learning and memory rather than to a withdrawal syndrome from stimulants.

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NICOTINE (TOBACCO)

Nicotine is one of the most addicting substances known. Indeed, the risk of becoming dependent on nicotine following any tobacco use is higher than the risk of becoming dependent on alcohol, cocaine, or marijuana following the use of those substances. Among multiple drug users, quitting tobacco use is often cited as more difficult than giving up alcohol or cocaine. Most current views of tobacco use include physiological addiction to nicotine as a factor in the difficult course of achieving smoking cessation.

Nicotine, the active ingredient in tobacco, shares characteristics with other addictive drugs. First, these drugs alter central nervous system function at specific receptors, and they often change the structure of these receptors. In addition, increases (up regulation) or decreases (down regulation) in receptor numbers occur. Second, repeated exposure to addictive drugs results in "tolerance," which means that the individual must progressively self-administer higher drug doses to obtain the same effects that initially occurred at lower doses. Third, as cellular and neurological functioning adapt to the continuous presence of these drugs, a state of physical or physiological dependence is produced. As a result of this dependence, the removal of any of these drugs is accompanied by feelings of emotional and physical discomfort and an inability to function normally. Finally, a hallmark of dependence-producing drugs is that they serve as biological reinforcers (rewards) for animals, including humans.

NICOTINE TOLERANCE AND DEPENDENCE

Nicotine is a pharmacologic agent that acts on the central nervous system. Specifically, it acts on cholinergic receptors in the brain. The cigarette is a very fast and effective delivery system for nicotine,

and effects occur rapidly after a single inhalation of tobacco smoke. Nicotine quickly crosses the blood-brain barrier and interacts with brain receptors. Nicotine alters moods and acts on pleasure-seeking receptors in the brain, including dopamine and serotonin. The nicotine alkaloid affects numerous body systems. It raises blood pressure and heart rate, for example, and it also affects the peripheral nervous system. Both stimulant and depressive effects are observed in cardiovascular, endocrine, gastrointestinal, and skeletal systems.

A person's initial exposure to nicotine may be an unpleasant experience, for it often causes sickness, intoxication, and disruptions in physiologic functioning. Among individuals presumed to be at greatest risk of becoming regular users of tobacco, the body quickly adapts to nicotine and the initial unpleasant effects become less pronounced. Thus, tolerance develops and physical dependence occurs. Smokers are free to self-administer the dose of nicotine they desire, and as their tolerance increases, they often increase tobacco use accordingly. The level of dependence is strongly related to the dose of nicotine.

As an individual becomes addicted to smoking, the smoker feels normal, comfortable, and effective when taking nicotine, but physically and emotionally uncomfortable and ineffective when deprived of nicotine. The development of dependence weakens the ability of the person to achieve and sustain even short-term abstinence. Thus, in the nicotine-dependent person, "normal" function depends on nicotine, and the removal of nicotine results in impairment.

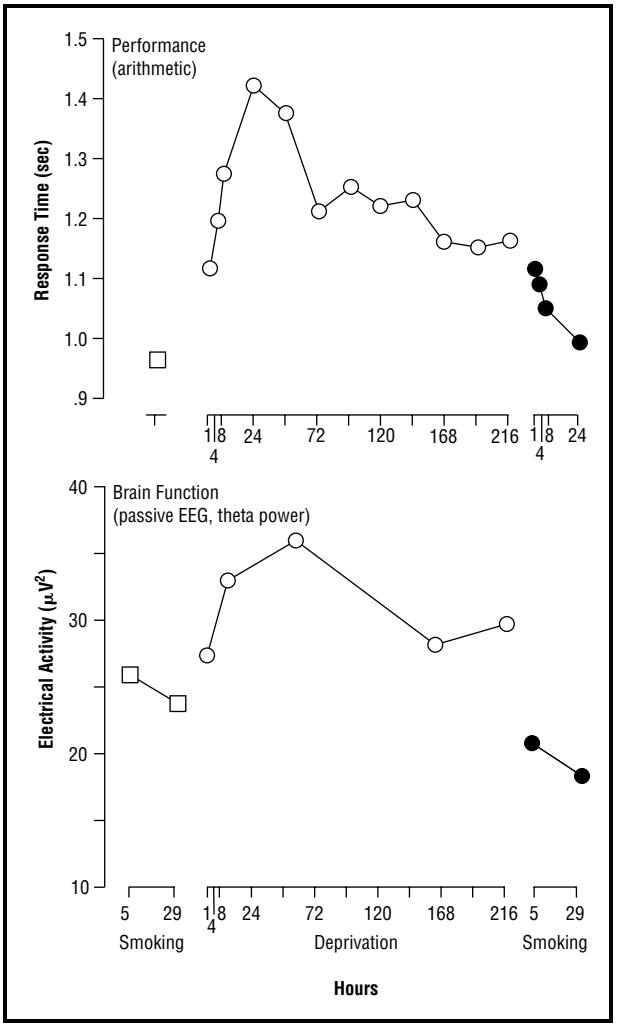

Figure 1. Cognitive performance and an electrophysiological measure of brain function during smoking and abstinence. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

NICOTINE WITHDRAWAL SYMPTOMS

The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*, recognizes nicotine dependence as a substance-related disorder, with a well-defined withdrawal syndrome (*DSM-IV-TR*, p. 265). The potential withdrawal symptoms include depressed mood, insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite or weight gain. These symptoms must cause significant distress or impairment in order to be diagnosable as withdrawal. The severity of the symptoms will depend on the severity of nicotine dependence. Evidence suggests that withdrawal may begin earlier than previously appreciated, with many symptoms emerging within one to three hours of nicotine abstinence. Withdrawal symptoms are strongest in the first few days after smoking cessation and usually diminish within a month, although some smokers may continue to experience withdrawal symptoms for many months.

There are a number of other effects of smoking cessation. There is evidence, for example, that cognitive ability is impaired when smoking cessation is attempted. The cognitive deficits are correlated with disruptions in brain electrophysiologic function. Figure 1 shows that deficits in an arithmetic task follow a similar time course as changes in the brain's electrical activity. These effects begin a few

hours after the last dose of nicotine, peak during the first few days of abstinence (when smokers trying to quit are most likely to relapse), and mostly subside within a few weeks. An impairment of sustained attention may set in even more quickly, with one study showing significant impairment after 30 minutes of abstinence. Another study of cognitive impairment, using four complex cognitive tasks during withdrawal from smoking in heavy smokers, ex-smokers, and those who had never smoked, assessed ability to perform those tasks; smokers with 12 hours of abstinence had the worst scores on the tasks.

Another symptom associated with withdrawal is a craving for cigarettes. This craving is strongly related to the degree of nicotine dependence. Frequent craving may last for six months, with some smokers reporting occasional episodes of craving even years after cessation, which is far longer than most of the other symptoms associated with tobacco withdrawal. Craving is a major obstacle to cessation and, together with other indicators of nicotine dependence, it is strongly related to relapse, with the majority of smokers who attempt to quit relapsing within the first week of cessation.

Although the foregoing symptoms are universal (albeit with some variation among individuals), some withdrawal symptoms are unique to individuals with specific characteristics. Smokers with a history of major depression, for example, are at some risk of having another depressive episode during the course of stopping smoking. Smokers with various forms of preexisting cognitive dysfunction (e.g., attention-deficit disorder, schizophrenia) may experience a resurgence of their cognitive deficits during nicotine withdrawal. Smokers with comorbid substance-use disorders such as alcohol dependence or illicit substance dependence are likely to have more severe withdrawal symptoms as they attempt to address more than one dependency.

While the withdrawal syndrome is undoubtedly biologically based, behavioral factors have a strong influence on smoking cessation. Cigarette smoking involves a number of rituals that become an integral part of the smoker's daily life, resulting in numerous individual, social, and environmental prompts to smoke. At the individual level, the smoker may associate a cup of coffee, the end of a meal, or watching television as a prompt to light a cigarette. Socially, being with friends or family members who smoke may represent other cues to smoke. Environmental stimuli, such as being in bars or other places where many people smoke, are also likely to reinforce the smoker's desire to smoke. Exposure to any of these cues to smoke may result in relapse.

MEASUREMENT AND TREATMENT OF NICOTINE WITHDRAWAL

Several scales are commonly used to measure withdrawal symptoms, including the Shiffman-Jarvik Withdrawal Scale, the Minnesota Withdrawal Scale, and the Wisconsin Smoking Withdrawal Scale. Each scale consists of a list of various withdrawal symptoms, along with instructions to rate the severity of each symptom. Of these scales, however, only the Wisconsin Smoking Withdrawal Scale utilizes the most recent diagnostic criteria for withdrawal symptoms included in the DSM-IV-TR.

Two pharmacologic approaches—nicotine replacement therapy and non-nicotine drugs—have been shown to reduce nicotine withdrawal symptoms. In addition, behavioral approaches have proven useful for managing symptoms associated with withdrawal.

Nicotine Replacement Therapy (NRT). The purpose of nicotine replacement is to substitute a safer and more controllable form of nicotine to the smoker to aid in cessation. Although nicotine replacement delivery systems vary, all attempt to reduce the amount of nicotine available during cessation, so that an individual is weaned from nicotine addiction more slowly. Three nicotine replacement therapies are available over-the-counter: nicotine polacrilex gum (Nicoderm, Nicorette DS, Nicotinell), nicotine lozenges (Commit) and the transdermal nicotine patch (Nicoderm CQ, Nicotrol, Habitrol). Two other delivery systems are available by prescription: an oral nicotine inhalation system (Nicotrol Inhaler, Nicorette Inhaler) and a nasal nicotine spray (Nicotrol NS). The effectiveness of each of the systems has been well established in randomized, controlled trials. The limited evidence comparing different forms of NRT shows them all to be equally efficacious. However, combining the patch with rapid delivery forms of NRT (i.e., gum, lozenge, nasal spray, or inhaler) has been shown to be more effective than a single type of NRT.

Non-nicotine Pharmacotherapy. A number of drug therapies have been approved to alleviate or reduce some of the discomfort that accompanies smoking cessation. The newest of these, varenicline (Chantix) was approved by the U.S. Food and Drug Administration in May 2006. This drug binds to the same brain receptors as nicotine, so that it blocks nicotine from having reinforcing effects, while simultaneously providing some stimulation to curb withdrawal symptoms. Its efficacy is well established, and early research has shown it to be more effective than bupropion (Zyban), another smoking cessation drug. Bupropion acts as an antidepressant, and it is often used for this purpose. However, it is effective in smokers who have no history of depression. Thus, other factors appear to be involved in the success of this drug in smoking cessation.

Another antidepressant, nortriptyline (Aventyl, Pamelor, Nortrilen) has also been shown to be useful for smoking cessation. Clonidine (Catapres), originally used to treat hypertension, appears to be modestly effective in blocking the cravings for nicotine, especially in women. Other pharmacologic therapies are being tested for their value in ameliorating the withdrawal symptoms associated with smoking cessation. These include mecamylamine (Inversine), which is thought to block the reinforcing action of nicotine, and anti-anxiety medications (such as benzodiazepines), which generally lower stress and decrease anxiety.

Behavioral Approaches. Behavioral approaches for preventing relapse have a long history of use in smoking cessation. Behavioral strategies generally focus on the social reinforcers of smoking. The most effective behavioral programs are those that have multiple components. Strategies for mitigating withdrawal include relaxation exercises (e.g., deep breathing), coping tactics (e.g., distracting oneself during periods of high craving), formation of social support networks (e.g., telling family and friends of your plans to quit), anticipation and avoidance of tempting situations (e.g., avoiding bars immediately after quitting if one associates drinking with smoking), simple messages to deal with withdrawal symptoms (e.g., reminding oneself that they are only temporary), and stimulus control (e.g., getting rid of ashtrays, having a smoke-free home). Multiple-component behavioral programs have been successful in helping smokers achieve cessation, and research suggests that nicotine replacement or pharmacologic approaches without a behavioral component have significantly lower success rates than those with a behavioral component. However, the addition of medications to behavioral treatment substantially increases quit rates compared with behavioral treatment alone.

WITHDRAWAL: NICOTINE (TOBACCO): SUMMARY

Nicotine is a very addictive drug that affects the central nervous system. Its use results in tolerance and dependence, so that the user feels most normal when using tobacco. A clear nicotine withdrawal syndrome is recognized; smokers attempting cessation may experience unpleasant or uncomfortable mood, insomnia, irritability, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite. Further, cognitive ability is somewhat impaired during cessation, strong craving for the drug is present, and powerful behavioral cues make cessation difficult. New approaches to the withdrawal syndrome include the administration of nicotine in a safer delivery system that can be tapered over time, and drugs to counter the unpleasant symptoms of withdrawal. Along with behavioral treatment, such pharmacologic tools may assist the smoker in achieving cessation.

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NONABUSED DRUGS

Although drug withdrawal is often considered synonymous with matters relating to drug abuse, a number of drugs that have no abuse potential and are prescribed for medical illness are associated with clear symptoms of withdrawal when their use is abruptly discontinued. The symptoms do not necessarily indicate drug dependence, a syndrome that has several features, including tolerance, inability to control drug use, and continued drug use despite deleterious effects.

CARDIOVASCULAR DRUGS

Beta-adrenergic blockers are taken by many people to treat hypertension (high blood pressure), angina pectoris (chest pain that occurs when the heart muscle is deprived of oxygen), heart arrhythmias following heart attack, and for migraine headache. The mechanism for each of these effects is related to the drug occupying the beta-adrenergic receptors in the blood vessels and the heart. When a patient abruptly stops taking a beta blocker, particularly when angina pectoris is the symptom being treated, a marked increase in the frequency and/or severity of angina pectoris may occur. This response occurs within the first few days of discontinuing the beta blocker; it may be prevented by slowly decreasing the drug dose over several days before completely stopping the drug. The discontinuation symptom is probably related to an increased sensitivity of the beta receptor to the body's own hormones norepinephrine and epinephrine, when its antagonist, the beta blocker, is suddenly removed. The withdrawal syndrome disappears in a few days.

Clonidine is used for hypertension and to treat withdrawal from opiate narcotics. Its mechanism of effect is stimulation of alpha (type 2)-adrenergic receptors in the central nervous system, which results in decreased stimulation of nerves that release norepinephrine and epinephrine in blood

vessels. When clonidine is abruptly stopped, blood pressure increases to well above baseline levels and may become dangerously high. This response occurs within one to two days after stopping the drug and is prevented by slowly (over several days) decreasing the drug dose before stopping it completely. The symptom may be due to a rebound over-stimulation of norepinephrine and epinephrine releasing nerves in blood vessels. This rebound hypertension disappears within a few days, again consistent with the time required for alpha-adrenergic receptor re-regulation.

Nitroglycerin and other nitrates are taken to treat angina pectoris. They cause the relaxation of blood vessels by the activation of an intracellular enzyme, guanylyl cyclase, which catalyzes formation of cyclic GMP (guanosine monophosphate). The coronary arteries (blood vessels that supply heart muscles) relax when exposed to nitrates. If the coronary arteries are blocked by atherosclerosis, causing insufficient blood supply to the heart, angina pectoris can occur. Relaxation of these arteries improves blood supply to the heart, and the chest pain rapidly disappears. When nitrates are taken continuously for relief of chest pain and then abruptly discontinued, rebound angina pectoris that is more frequent or more severe than the angina experienced prior to treatment may occur. This symptom begins within a few hours of the last nitrate dose and in a time course consistent with the metabolism and removal of the nitrate drug from the body. If the nitrate dose is slowly decreased before discontinuation, the rebound angina may be prevented. The mechanism for this withdrawal syndrome is not known.

NEUROPSYCHOPHARMACOLOGICAL DRUGS

Abrupt discontinuation of any of the major classes of antidepressants may result in discontinuation reactions. Antidepressants vary in their ability to cause reactions, and reactions are more common after abrupt discontinuation and longer courses of treatment. Common symptoms include gastrointestinal problems such as nausea, abdominal pain, and diarrhea. In addition, some patients complain of a flu-like illness consisting of weakness, chills, fatigue, headaches, and muscle aches. Central nervous system dysfunction characterized by difficulty falling asleep, anxiety, vivid dreams or nightmares, or jitteriness can also occur, as can such affective symptoms such as irritability and low mood. Symptoms usually start a few days after termination of the antidepressant and continue for between one day and three weeks. Selective serotonin reuptake inhibitors (SSRIs), a class of antidepressants, have several distinct discontinuation symptoms, including dizziness and such sensory abnormalities as electric shock-like sensations, numbness, and paresthesia. The symptoms typically go away the day after antidepressant treatment has resumed. To reduce the risk of withdrawal symptoms, some physicians have recommended that antidepressants be gradually reduced over a four-week period rather than abruptly discontinued.

Monoamine oxidase inhibitor (MAOI) antidepressant drugs interfere with the enzymatic breakdown of neurotransmitters (such as norepinephrine) in the brain. Sudden discontinuation after high chronic dosing has been associated with psychosis (including visual hallucinations) and delirium (with agitation and mental confusion). Milder symptoms consisting of anxiety, vivid dreaming, or nightmares may also occur. The exact mechanism of withdrawal had not been well studied as of 2008, but it was suspected to relate to the way nerve cells regulate the release of neurotransmitters in the brain.

Antipsychotic agents are commonly used in psychiatric practice for the treatment of psychotic disorders such as schizophrenia. These agents all block brain dopaminergic receptors—the basis for their effectiveness in treating psychotic illness. These agents also inhibit emesis (vomiting) by blocking dopamine in the brain. Chronic dopamine blockade results in increased numbers of these receptors. The abrupt discontinuation of this class of drugs results in nausea, vomiting, and headaches. The antipsychotic and antiparkinsonian effects of neuroleptics are also still present for a prolonged period. According to some research, it is not known whether the prolonged effects of neuroleptic drugs in humans are due to the continued presence of drug in brain tissue or to long-lasting, drug-induced physiologic changes.

Clozapine is in a class of atypical antipsychotic drugs associated with discontinuation symptoms. Although atypical antipsychotics may be different from other drugs used to treat psychosis, there are also significant differences among these drugs in their effects on the receptors of the central nervous

system. Clozapine interacts with a wide range of neurotransmitter receptors, especially serotonin receptors. Common discontinuation symptoms of clozapine include delusions, hallucinations, hostility, and paranoia. The underlying mechanism of these symptoms is thought to be supersensitivity of the cholinergic receptor (i.e., the muscarinic acetylcholine receptor, one of the main receptors for cholinergic neurotransmission in the central nervous system).

OTHER DRUGS

Baclofen, a muscle relaxant, is used to treat muscle spasticity associated with certain paralytic states. It acts as an agonist (mimic) of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA). Therefore, baclofen inhibits excitatory neural pathways, which are modulated by GABA. This is a rather selective effect as there are two types of GABA receptors and pathways, GABA-A and GABA-B, and baclofen only acts on GABA-B receptors. The symptoms experienced by a person suddenly discontinuing baclofen may include auditory and visual hallucinations, severe anxiety, increased heart rate and blood pressure, delirium, and generalized seizures. Such clinical symptoms are consistent with the impaired modulation of neural-excitatory pathways. When the dosage of baclofen is gradually reduced before discontinuation, these symptoms either do not occur or are attenuated.

In mimicking the endogenous corticosteroid cortisol, corticosteroids signal the pituitary gland to stop the synthesis and release of the adrenocorticotrophic hormone (ACTH) and, perhaps, the hypothalamus to stop the release of the corticotropin-releasing hormone (CRH). ACTH release from the pituitary, which normally stimulates the adrenal glands to produce corticosteroids and which is modulated by the hypothalamic CRH, is blocked by exogenous corticosteroids. Adrenal production of cortisol decreases and the adrenal glands atrophy. When corticosteroid therapy is abruptly discontinued, the atrophic adrenal glands no longer respond to ACTH stimulation, so the patient has symptoms of adrenal insufficiency. Clinically, this condition is manifested by fatigue, weakness, electrolyte imbalance, and the lack of many bodily responses to stress. If an individual remains in this state for more than a few hours, severe illness and death can be expected. When the adrenal glands become atrophic during long-term corticosteroid treatment, discontinuation must be done slowly, with the dose decreased gradually over many weeks to permit the adrenal glands sufficient time to be restored to their normal size under the influence of ACTH stimulation and to have sufficient stores of the body's own cortisol to respond to stress in a physiologically appropriate manner.

Human physiology is characterized by the coordinated and finely tuned operation of multiple messaging systems, exhibiting both positive and negative feedback regulation, with multiple levels of control. All the drugs mentioned exert both their desired and undesired effects by interfering with these systems. In the drug-treated individual, homeostasis is maintained by counteracting some of the drug effects at the cellular level. However, such adaptation is not without cost. Sudden discontinuation of a drug to which the nervous system has adapted can produce a period of disequilibrium between the affected messaging systems. The disturbed physiology is expressed by withdrawal symptoms that are specific to the systems involved.

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WOMAN'S CHRISTIAN TEMPERANCE UNION. The nineteenth century was a time of drastic changes in the way many Americans viewed alcohol. Early in the century, on average, U.S. citizens each consumed approximately 7 gallons of alcohol annually, the equivalent of about 2.5 ounces of pure alcohol daily. Concern that the United States would turn into a "nation of drunkards" sparked the temperance movement of the early nineteenth century. This movement was loosely organized, consisting of diverse factions: (a) neorepublicans, who were concerned with a host of problems that threatened the nation's security; (b) temperance societies, such as the Washingtonians, which served as the forerunners of modern-day self-help groups; (c) local women's groups that organized spontaneous protests against saloonkeepers from the 1830s on; and (d) physicians, who came to view habitual drunkenness as a disease called "inebriety." The goals of these groups varied; they ranged from helping habitual drunkards, to discouraging the use of alcoholic beverages, to advocating prohibition of alcoholic beverages, to signing pledges to abstain from drink, and to closure of saloons.

This first wave of temperance activists met with some success: 13 states passed prohibition laws by 1855, and average alcohol consumption rates dropped to less than 3 gallons per person annually. Momentum slowed during the Civil War, but the early movement set the stage for the post-Civil War temperance movement. Physicians formed the American Association for the Cure of Inebriety in 1870, an organization advocating medical treatment for "inebriety" in asylums specifically built for that purpose, according to William L. White (1998).

Many Americans experienced the years following the Civil War as a chaotic time of rapid social and technological change during which many sought what Mark E. Lender and James K. Martin (1982, p. 92) term "a search for order." Broad-based social reform movements attacked a number of issues. Paul Aaron and David Musto (1981) refer to this period as the second great prohibition wave. Although the Washingtonians were in decline by 1845, evangelical Christians formed fraternal societies based on "gospel temperance" (Chavigny, 2004, p. 113). Many local temperance societies survived the Civil War, as did the American Temperance Union. In 1869 the National Prohibition party formed to support the abolition of alcohol. The National Prohibition party recruited women into the organized fight against liquor and advocated complete and unrestricted suffrage for women.

The post–Civil War Progressive movement also influenced the issue of temperance. The Progressives believed that alcohol was "the enemy of industrial efficiency, a threat to the working of democratic government, the abettor of poverty and disease" (Bordin, 1981, p. xvi). To the Progressives, temperance reform was a means for confronting genuine social problems. Business leaders increasingly came to view the use of alcohol as incongruous with the new technological society

that America was becoming. Alcohol symbolized wastefulness, rampant pluralism, individualism, and potential social disorder.

At the same time, a growing number of physicians and temperance workers began to regard habitual drunkenness as an inherently progressive disease. According to their "stepping stone" theory, even moderate drinking inevitably led to addiction. As long as liquor was available, people would be enticed to drink. As long as moderate drinkers were around to act as models, then there would be drunkards. Increasingly, the blame for addiction to alcohol was placed less on the individual and more on the society that permitted the sale of liquor, tolerated saloons, and condoned drinking.

The women's temperance movement developed in a context that included better education for women, a declining birth rate, and growing urbanization. Women were portrayed as the moral guardians of society and protectors of the home, and increasingly, alcohol was seen as a threat to moral values and to the security of the home. These factors, combined with a larger middle class and better communications, set the stage for the first mass movement of women into U.S. politics.

THE WOMEN'S CRUSADE

Ironically, the direct origins of the movement through which women gained entry into the political arena can be traced back to a man, Dio Lewis. As a child, Lewis witnessed his mother organize a protest against a saloonkeeper in Clarkesville, New York. This protest was similar to the many confrontations between groups of women and saloonkeepers across New England and the Midwest. In the 1850s and 1860s, lectures by Dio Lewis persuaded women to organize similar campaigns, according to Barbara L. Epstein (1981, pp. 93–95). By the 1870s Lewis, a trained homeopathic physician, had given up his medical practice and embarked full-time on the lecture circuit. In December 1873 Lewis's lecture in Hillsboro, Ohio, instigated a grass-roots movement that came to be known as the Women's Crusade.

The Women's Crusade quickly moved through Ohio and into neighboring states. Typically, the women of a community called a meeting eliciting support from other women. After praying over their cause, they organized their efforts, which included asking local ministers to preach on the topic of temperance and seeking pledges of support from local political leaders. Finally, they took to the streets, marching on distributors of liquor, in an attempt to persuade them to cease their sales of alcohol.

HISTORY OF THE WCTU

By November 1874 the Women's Crusade had grown to the point that they called a national convention. Sixteen states were represented at this convention, out of which the Woman's Christian Temperance Union (WCTU) emerged. Annie Wittenmyer was named the first president of the WCTU. Wittenmyer gained leadership experience in the Sanitary Commission during the Civil War, an organization that was the forerunner of the American Red Cross. The WCTU platform of action included the principle of total abstinence for members and a commitment (a) to introduce temperance education in both Sunday schools and public schools; (b) to continue to use the evangelical methods, mass meetings, and prayer services that had been successful during the Women's Crusades; (c) to urge newspapers to report on their activities; and (d) to distribute literature informing people of their cause.

1874–1879. Under the leadership of Annie Wittenmyer, the primary commitment of the WCTU was to gospel temperance. Wittenmyer contended that the WCTU program should stress personal reform and religious conversion of the drunkard and of the whole liquor industry by moral suasion. Under her leadership the WCTU committed to a "singleness of purpose" that shied away from seeking legislative mandates as the solution to intemperance (Wittenmyer, 1877). This commitment also led Wittenmyer to distance herself and the organization from the women's suffrage movement; she feared possible repercussions for women *in the home*, should they campaign for the right to vote. In 1876 Frances Willard introduced the concept of "home protection" to the WCTU, building on notions of women's traditional roles within the home and the need to defend and protect those roles,

Although Wittenmyer's single-minded goal of abstinence was instrumental in the WCTU's early success, the movement soon widened to embrace a

broader set of goals and objectives under the leadership of Willard, chosen as the national secretary at the first convention. Succeeding Wittenmyer as president in 1879, Willard served in that role until her death in 1898 and is recognized as the most influential leader of the women's temperance movement. Some observers of the women's temperance movement may be more familiar with the name of Carrie Nation, who was known for raiding saloons armed with axes and hatchets; however, militant individuals such as Nation constituted a small fringe element of the WCTU. During the latter part of the nineteenth century, the true spirit of the WCTU was embodied in the person of Frances Willard.

1879–1898. While Wittenmyer's primary commitment was to moral suasion, Willard held more radical views on women's rights and industrial practice. Willard pushed the WCTU into broader commitments to other social reforms. Taking up Wittenmyer's narrower concept of "home protection," Willard proposed extending women the right to vote on prohibition issues as a means of further protecting women. The idea of granting women the right to vote based on their natural or political right to do so was *not* palatable to many people, women and men alike. By introducing the suffrage issue under the guise of home protection, Willard introduced the right-to-vote issue within the WCTU with less opposition than if she had sought solely to address women's suffrage.

As president, Willard emphasized organization at the local level, establishing the mass base necessary for effective action. By 1880 the WCTU easily outstripped other women's organizations in both size and importance. Ruth Bordin (1981) estimates that there were 1,200 local unions with 27,000 WCTU members by the time Willard became president. From 1882 to 1902 the WCTU was able to establish laws in every state compelling temperance education in schools, according to Joseph R. Gusfield (1986, p. 86).

Under Willard's leadership, the WCTU continued many of the programs that Wittenmyer had begun. The push for abstinence from alcoholic beverages typified the movement's goals. The WCTU of the 1880s, however, also departed from its roots, evolving from a temperance praying society to an activist organization. Whereas Wittenmyer sought change through moral suasion, Willard saw the advantages of political solutions to the problems caused by intemperance as well as the problems facing women. She supported federal constitutional prohibition as the most effective way to deal with alcohol abuse, endorsing the temperance ballot for women as the surest way to achieve prohibition.

By the mid-1880s the WCTU had expanded to every U.S. state and territory, and its platform had undergone similar expansion. Willard adopted the slogan "Do Everything" to describe the expanded activities of the WCTU under her guidance; initially, she had coined this phrase to depict the lengths to which she was willing to go to support the prohibition cause. The WCTU was internally organized into departments that illustrate the scope of activities: the Department of Scientific Temperance Instruction provided the first antidrug education and prevention programs in schools; the Department for Temperance Work among Negroes and Foreigners connected temperance to immigration, labor, and civil rights issues; and the Department of Health and Hygiene educated women about the need for exercise, comfortable dress, and proper diet (Epstein, 1981, p. 124).

The membership of the WCTU in the early 1890s grew to an estimated 150,000 dues-paying members, with an additional 150,000 in affiliated groups. From its original base among white, middle-class women, the WCTU reached out to women of all social classes and minority groups. The growing influence of the WCTU was evident in the passage of several state prohibition laws in the 1880s as well as in the growing support for a federal constitutional prohibition of liquor.

Although the number of women involved in the WCTU numbered approximately 1.5 million in the early twentieth century, the organization had begun to lose its power and importance. Most notably, Willard became less visible in the years preceding her death, and conflicts arose among other leaders as to the organization's proper direction. When older leaders withdrew from active participation, fewer young women replaced them. However, the WCTU remained dominant in the content of school-based anti-alcohol education programs and textbooks well into the twentieth century (Gusfield, 1986, p. 86, n. 44).

1898–2000s. Other prominent organizations endorsed women's rights and/or prohibition in the early twentieth century as membership in the WCTU slowly dwindled. Following Willard's death in 1898, the WCTU returned to a single-issue approach, focusing solely on prohibition. However, it was not until the growth of the Anti-Saloon League (established 1896) that national prohibition was realized. The Eighteenth Amendment to the U.S. Constitution was proposed and sent to the states on December 18, 1917, and was ratified by three-quarters of the states by January 16, 1919; it became effective January 16, 1920, prohibiting the manufacture, sale, or transportation of intoxicating liquors, for beverage purposes. During the 1920s the enforcement of prohibition was almost impossible in the face of pressure from the alcohol-beverage industry and because Americans would not easily give up drinking. The Repeal of Prohibition culminated in the Twenty-first Amendment to the U.S. Constitution; it was proposed and sent to the states February 20, 1933, and was ratified December 5, 1933.

Small groups of WCTU members can still be found in, for the most part, rural areas of the United States. Based in Evanston, Illinois, the organization can be considered among the forerunners of the "abstinence-only" movement, the "Just Say No" campaigns of the Reagan era, and other attempts to persuade more Americans to pledge abstinence.

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WOMEN AND SUBSTANCE ABUSE.

Each year 9 million women in the United States use illicit drugs. Another 3.7 million women use prescription drugs in non-prescribed ways. Gender differences in the prevalence of substance abuse reflect a combination of social, cultural, economic, and neurobiological differences. Women use the same psychoactive substances as men, but women use drugs in ways that lead them to experience different neurochemical and physiological effects than do their male counterparts. Unlike men, women's perceptions of well-being increase after they ingest alcohol, nicotine or tobacco, and cocaine, according to James A. Fallon et al. (2005) and Elinore McCance-Katz et al. (2005).

Historically, women have been differentially involved with alcohol, tobacco, illegal drugs, and prescription drugs. Before the Harrison Narcotic Act of 1914, the typical opiate addict in the United States was a white, middle-aged, middle- or upper-class woman addicted to medically prescribed drugs or nonprescription patent medicines. As changes in medical practice led physicians to cease overprescribing narcotics, David T. Courtwright (2001)

notes that this pattern began to decline even before the Harrison Act. Overall levels of opiate use declined dramatically in the early twentieth century, and women were not recruited into the ranks of heroin users at the same rates as men.

Systematic studies of gender-specific differences in the causes and consequences of substance abuse emerged only after the mid-1970s. In the latter decades of the twentieth century, drug use by pregnant and parenting women attracted increasing concern, despite this population comprising but a small part of the overall drug-using population. In the early twenty-first century overall rates of substance abuse remained about twice as high for men (12.3%) as for women (6.3%). However, the rates are similar (8%) in boys and girls ages 12 to 17 years of age (all statistics are from the National Household Survey on Drug Abuse 2006 unless otherwise indicated).

ALCOHOL AND TOBACCO USE

Although surveys of the U.S. population indicate that fewer women drink than men and women who do drink consume less alcohol than men, the gender gap narrowed during the twentieth century. Drinking rates rose slowly after the repeal of Prohibition. By 1940 only 38 percent of adult women drank compared to 64 percent of men; by 1965 consumption rates had increased, with 60 percent of adult women and 77 percent of men drinking (Golden, 2005, p. 44). However, consumption rates say little about problem drinking. Until recently little was known about women's alcoholism, but national surveys under way since the 1970s show that women comprise less than one-third of the estimated 17 million alcohol-abusing or alcohol-dependent individuals in the United States. The 2006 National Household Survey on Drug Abuse (NHSDA) showed 57 percent of men reporting drinking alcoholic beverages in the previous month,

Although some have suggested that social norms regarding male and female drinking may converge, there is little evidence of increased female alcoholism or problem drinking. AP IMAGES

compared with 45 percent of women. The NHSDA defines heavy alcohol use as five or more drinks per day on five or more days in the past month. By this definition men are much more likely than women to be heavy drinkers (approximately 10% and 2%, respectively).

Although some have suggested that social norms regarding male and female drinking may converge, there is little epidemiological evidence of increased female alcoholism or problem drinking. Changing female drinking patterns have resulted more in a reduction in female abstainers than an increase in problem drinkers. The smallest sex differences are found among the youngest cohorts (with 7.9% of boys and 4.3% of girls aged 12 to 20 drinking heavily in 2006). Among adults aged 35 and older, men are eight times as likely as women to be heavy drinkers (8% compared with 1%).

There is evidence of sex-role convergence in tobacco use. In 1955, 52 percent of adult men smoked, compared with 25 percent of adult women. Since then, the proportion of men who smoke has decreased markedly while rates among women have held fairly steady. Among those aged 12 or older in 2006, 27 percent of men and 22 percent of women were current smokers. Among youths aged 12 to 17, girls and boys differ little in rates of current cigarette use (10% of girls and boys). Overall adolescent smoking has declined due to increased perceptions of health risks associated with smoking (NHSDA, 2006).

Tobacco companies have targeted advertising to make smoking attractive to young women. Once they begin smoking, women typically have a harder time quitting. Smoking-related health problems such as lung cancer have increased among women since the 1970s. Lung cancer now surpasses breast cancer as the leading cause of cancer deaths among women.

ILLICIT DRUG USE

Approximately 40 percent of women report using an illicit drug at some point in their lives and, in 2006, 6.2 percent of women aged 12 and older reported using one in the past month. In 2004 approximately 14 percent of those arrested for drug-abuse violations were female. Males, however, are more likely than females to be arrested for possessing or selling illicit drugs. From 2001 to 2005 women's arrest rates for drug abuse violations increased dramatically despite the fact that males are more likely than females to use illicit drugs. Gender differences are smallest among adolescents aged 12 to 17 and among adults aged 35 and older and largest among young adults aged 18 to 34, the age range in which illicit-drug use is most prevalent. Among both men and women, marijuana is the most frequently used illicit substance, with more than 35 percent of high school females reporting use in 2005.

Early research on illicit drug-using women tended to focus on sexuality, pregnancy, or fetal and neonatal development. This trend was pronounced in the 1980s when women's use of cocaine and crack-cocaine was on the rise (Murphy & Rosenbaum, 1999, p. 7). Since then cocaine use has decreased, and sex differences in regular cocaine use are small even in young adults, among whom cocaine use is most common. Crack-cocaine posed a specific problem for women, bringing them into the criminal justice system in ever-greater numbers. Between 1980 and 1992 the number of women in prison tripled due largely to patterns of drug arrests and sentencing (Kandall, 1996, p. 252).

Although heroin use became quite rare in the United States in the last three decades of the twentieth century, media attention to the problems of women and crack-cocaine overshadowed the fact that women continued to struggle with opiates. By the early 1990s women comprised nearly one-third of patients in methadone clinics in New York state (Kandall, 1996).

PRESCRIPTION DRUG ABUSE

In the 1970s feminist scholars drew attention to the overmedication of women with psychoactive drugs. These early critiques derived from content analyses of sex-stereotyped advertisements in medical publications. Most ads for prescription psychoactives depicted woman patients, and survey research on representative populations confirmed that women were using more of these drugs than were men. Concerned that psychoactive drugs were being used as a subtle form of social control, critics charged that physicians were prescribing tranquilizers and antidepressants to alleviate women's

normal life transitions, such as menopause, college attendance, or empty-nest syndrome, as well as women's discontent with limiting and inequitable sex roles.

Some prescription psychoactives have dangerous long-term side effects and a high potential for producing dependency. Further, since women also use more over-the-counter medications and women's alcohol problems often go undetected by physicians, women who use prescription psychoactive drugs are vulnerable to adverse drug interactions. Alcohol in combination with other substances is the most frequent cause of emergency-room episodes in the Drug Abuse Warning Network (DAWN) system. Although women drink less and are less likely to use illicit drugs, they have equaled or exceeded men in drug-related emergency room episodes since the mid-1980s due to tranquilizer, sedative, and analgesic use.

Abuse of prescription painkillers such as Vicodin and OxyContin and stimulants such as Ritalin increased in the 1990s as these drugs became more available through Internet sales and diversion to the illegal market. Although men and women use prescription drugs nonmedically at similar rates, women are more likely than men to suffer from co-morbidities that accompany substance abuse such as depression, anxiety, and trauma. Girls and women report using drugs to cope with stressful life events, and doctors are more likely to prescribe narcotics and anti-anxiety medications for females than males in conjunction with these events. In the youngest study group, girls ages 12 to 17 are more likely than boys to abuse psychotherapeutic drugs, including stimulants (NSDUH, 2006).

GENDER DIFFERENCES IN SUBSTANCE ABUSE

Studies of adolescents generally find similar correlates of substance abuse among both boys and girls. The strongest predictor of adolescent alcohol, tobacco, and illicit-drug use is having friends who use alcohol, tobacco, and drugs. Other factors that predict substance abuse by peers include parental substance abuse, poor academic performance, and low commitment to educational pursuits.

Researchers have identified some gender differences in the development of alcohol and drug problems. Relationship issues are salient in the etiology of female substance abuse. Alcoholism in women is more strongly correlated with family history than is alcoholism in men. Girls and women are likely to be introduced to alcohol or illicit drugs by a boyfriend or spouse, and female alcohol or drug dependence may develop in the context of such relationships.

Alcohol and drug abuse are more often associated with depression in girls and women than in males. It is unclear whether depression is a cause or a consequence of substance abuse among girls and women. Women in treatment for substance abuse are more likely than men to say their problem with drinking or drug abuse developed after a life crisis, trauma, or tragedy such as the death of a family member. A sizable proportion of women in treatment report histories of sexual abuse.

Some believe these different attributions and recollections reflect genuine sex differences in the etiology or causation of substance abuse. Others caution that the greater stigma attached to female substance abuse may motivate women to develop socially acceptable explanations, such as personal crises and emotional difficulties, for their problem drinking or drug use. The course of problem drinking and drug addiction varies by gender. Women entering treatment for alcoholism or drug abuse tend to have begun heavy drinking or drug use at a later age, on average, compared with men entering treatment. The term *telescoping* has been used to describe women's rapid progression from controlled alcohol or drug use to alcohol and drug dependency.

EFFECT OF SUBSTANCE ABUSE BY GENDER

For many reasons alcohol and drug abuse produce more deleterious social, economic, and health consequences among women than among men. Women metabolize alcohol and drugs differently due to their lower ratio of water to total body weight. When equivalent alcohol is consumed, more alcohol passes into a woman's bloodstream, so women reach higher peak blood alcohol concentrations than men. Liver disease progresses more rapidly in women, and they are more prone to alcohol-related brain damage, exhibiting physical brain abnormalities and cognitive deficits after a shorter drinking history as compared to men. Drugs such as marijuana that are deposited in body

fat may have slower clearance rates in women, creating potential cumulative toxicity and adverse drug and alcohol interactions. Such physiological differences are compounded by social settings in which women drink or use drugs that render them vulnerable to violence and/or sexual abuse and hasten the onset of physical health consequences.

Women diagnosed as alcoholic have very high mortality rates relative to both the general population of women and to alcoholic men. Although deaths due to drugs other than alcohol and tobacco are relatively uncommon among women, overdose death rates among women began to climb from 1999 to 2004. Nevertheless, men remain twice as likely to die from overdoses of sedatives, prescription painkillers, and illicit narcotics such as heroin. According to the Centers for Disease Control, accidental drug overdose ranks just below traffic fatalities as the leading cause of preventable deaths in the United States

Social and biological factors place women at risk for contracting HIV, the virus that causes AIDS via infected blood and semen. Social practices like sharing needles or having sexual relations with intravenous (IV) drug users places both men and women at risk, although there is some evidence for women's greater biological vulnerability for contracting AIDS during any given sexual encounter. Most AIDS cases have resulted from transmission of HIV during intimate sexual contact between men who have sex with men; between 2001 and 2004 only 17 percent of all AIDS cases involved IV drug use as a route of transmission. When women contract AIDS, the most common route of transmission is through their own IV drug use or sexual contact with an IV-drug-using partner. Racial and ethnic minorities have been disproportionately affected by HIV/AIDS. In 2004 AIDS case rates were seven times higher among African American men than among white men and 21 times higher among African American women than among white women (Centers for Disease Control and Prevention, 2007).

Women's social roles as mothers and their reproductive functions increase alcohol- and drug-related health risks to children and fetuses. Alcohol, tobacco smoking, and drug abuse are associated with female reproductive disorders including breast cancer, amenorrhea, failure to ovulate, atrophy of the ovaries, miscarriage, low birth weight, and early menopause. Although men also experience reproductive and sexual difficulties as a result of alcohol and drug abuse, including erectile dysfunction, low testosterone levels, testicular atrophy, and diminished sexual interest; little attention has been focused on these problems. Surveys in 2002 and 2004 revealed that 109,000 pregnant women abused pain relievers in the past year. Past-year abuse of legal and illegal stimulants and sedatives/tranquilizers was reported by 32,000 and 56,000 pregnant women, respectively (NSDUH, 2006).

Infants born to women who used alcohol, tobacco, or other drugs during pregnancy can experience numerous health problems, including low birth weight, major congenital malformations, neurological problems, and withdrawal symptoms. Although substance abuse at any time during pregnancy can cause birth defects, rapid cell division in the first weeks of embryonic development means the teratogenic (capable of interfering with fetal development) effects of alcohol and drugs are generally greatest early in pregnancy, before women even realize they are pregnant. Despite the difficulty of establishing criminal intent if substance abuse occurred early in an unintended or unrecognized pregnancy, some state legislatures and courts have tried to terminate women's parental rights when newborns tested positive for drug or alcohol exposure. Beginning in the 1980s some jurisdictions charged mothers who used alcohol or drugs during pregnancy with child abuse, neglect, or delivery of a controlled substance to a minor. Critics charge that such policies deter women from prenatal care and drug treatment. Disentangling alcohol or drug effects from other adverse conditions such as poverty, poor nutrition, acute or chronic illness, and inadequate prenatal care is difficult. Prenatal drug-use screening raises important questions of fairness because hospitals and clinics serving poor and minority patient populations are more likely to detect prenatal substance abuse despite evidence that substance abuse occurs in all socioeconomic categories.

Gender differences in the effects of substance abuse are the combined product of different social expectations and norms that govern drinking and drug use. Male substance use is less socially

controlled—occurring more often in recreational contexts, public places, and all-male settings—whereas female substance use more likely occurs in the home, with a male partner, or under medical auspices. Despite women's greater biological vulnerability and the social stigma associated with female alcohol and drug abuse, men are still more likely to experience problems with social functioning related to heavy drinking and illicit drug use. Women's substance abuse is more strongly associated with intrapsychic problems. Advocates have sought to expand drug treatment for women and create programs that address gender-specific needs.

GENDER AND SUBSTANCE ABUSE TREATMENT

Despite recognition that women alcoholics and drug abusers have gender-specific treatment needs, men outnumber women in drug and alcoholism treatment units. According to the 2006 National Survey on Drug Use and Health, approximately 4 million people (representing 1.6% of the population) in the United States received substance abuse or alcoholism treatment. Women account for approximately 30 percent of treatment admissions; and repeated surveys since the 1970s have demonstrated that women's need for treatment outstrips the quantity of treatment slots available (NSDUH, 2006).

Historically, substance abuse treatment programs have been geared more to the problems and needs of male clients. Recent attention to the history of trauma, including sexual abuse and domestic violence, has emerged in treatment contexts with findings that many women substance abusers have been diagnosed with posttraumatic stress disorder (PTSD). Advocates urge treatment programs to address women's histories of physical and sexual abuse, domestic violence, and relationships with substance-abusing partners.

Among alcoholics and addicts, a greater percentage of women are parents; and among substance-abusing parents, more mothers have child custody than fathers. Concern that they will lose custody remains a major barrier to women seeking substance-abuse treatment. Few residential treatment programs make provisions for child care. Many women are unable to find caregivers for their children if they enter residential treatment and fear permanent loss of custody of their children to foster care. Incarcerated women, who retain custody at much higher levels than their male counterparts, face the dearth of drug treatment in prison as well as social intolerance and stigma.

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WOOD ALCOHOL. *See* Methanol.

WORLD HEALTH ORGANIZATION EXPERT COMMITTEE ON DRUG DEPENDENCE.

The World Health Organization (WHO) originated from a proposal at the first United Nations (UN) conference held in San Francisco in 1945 that "a specialized agency be created to deal with all matters related to health." This proposal resulted in a draft WHO constitution signed by sixty-one governments at an international health conference held in New York City in 1946. The constitution was subsequently ratified by the twenty-six member states of the UN and came into force on April 7, 1948. The enormous proposed scope of WHO led to the early concept of Expert Committees, and they have become an essential part of the machinery of the organization. Their function is to give technical advice to WHO. Members of these committees are "appointed by the Director-General, in accordance with regulations established by the Executive Board." The members are chosen for their "abilities and technical experience" with "due regard being paid to adequate geographical distribution." Reports of expert committees can only be published with the authorization of the World Health Assembly or the WHO executive board.

One of the first tasks of the UN and WHO was to take over the regulatory work on addiction-producing drugs that had been initiated and carried out by the League of Nations. Thus, the Expert Committee on Habit-Forming Drugs was established in 1948 to provide expert technical advice to the UN Permanent Central Opium Board and Drug Supervisory Body and the Division of Narcotic Drugs. The first meeting of the expert committee was held January 24–29, 1949, at the Palais des Nations in Geneva, Switzerland, where it continued to meet until the WHO building opened in 1961. The expert committee, in its report on the second session, felt that the expression *habit forming* was no longer appropriate and recommended that the designation of the committee be changed to Expert Committee on Drugs Liable to Produce Addiction. This change was adopted by the WHO executive board at its fifth session and remained until 1964, when it was altered to Expert Committee on Dependence Producing Drugs and finally in 1968 to its present designation, Expert Committee on Drug Dependence.

In its early years, the expert committee reported directly to the director-general of WHO through its own secretary. In 1965 it became part of the Division of Pharmacology and Toxicology. From its inception to 1972, the Secretariat was mainly in the hands of Dr. Hans Halbach. In 1977 the expert committee became part of the Division of Mental Health, under the direction of Dr. Inayat Khan, where it remained until 1990 when a new Programme on Substance Abuse was created.

The early meetings of the expert committee were mainly devoted to the opioids—including the natural products, semisynthetics, and synthetics. The committee responded to notifications on specific compounds by individual nations and made recommendations as to international control, which they communicated to the secretary-general of the UN. Often-recurring discussions began concerning definitions, methods for evaluating dependence liability in animals and humans, the need for accurate epidemiological data concerning the extent of abuse, and public health problems associated with drugs in general and of specific compounds in particular. During this period, the expert committee had an important consultative role in developing a new international drug-control treaty, the result of an international conference held in New York City in January 1961. From this Conference emerged the Single Convention on Narcotic Drugs, 1961. This convention was amended in 1972, again with strong input from the expert committee, and remains the early twenty-first century instrument for international control of opioids, cocaine, and cannabis (marijuana).

The committee's concern for the potential abuse of the newly emerging ataractics (tranquilizing drugs)

Meeting	Considerations
19th meeting, 1972	• Discussed the current status of the epidemiological study of drug dependence
20th meeting, 1973	• Primarily concerned with the topic of prevention • Reviewed the literature
21st meeting, 1977	• Mainly a convention on psychotropic substances • Considered appropriate pharmacological studies in animals and humans • Assessed public health and social problems • Assessed therapeutic usefulness, the problem of chemically generic extensions to the list of scheduled substances and the decision-making process • Recommendations made on international cooperation • Collection of data deemed necessary to make decisions on controlling substances
22nd meeting, 1985	• Implemented new procedures for review of substances approved by the WHO Executive Board • Considered twenty-eight phenethylamines for control • Requested more and better epidemiological data and more consideration of structure-activity relationships, isomeric state and drug metabolism
23rd meeting, 1986	• Reviewed thirty-one barbiturates
24th meeting, 1987	• Rejected control of seven nonbarbiturate sedative hypnotics • Considered the marked increase in the illicit trafficking of secobarbital • Recommended control of a number of fentanyl and meperidine analogs
25th meeting, 1988	• Recommended control of four additional nonbarbiturate sedative hypnotics including methaqualone • Revisited the opioid agonist-antagonist analgesics and recommended that buprenorphine and pentazocine be controlled under Schedule III of the Psychotropic Convention
26th meeting, 1989	• Considered four additional uncontrolled benzodiazepines and recommended control for one
27th meeting, 1990	• Devoted to the scheduling of the benzodiazepines as a class • Recommended that WHO keep diazepam and flunitrazepam under surveillance
28th meeting, 1992	• Recommended requesting the integration of substance misuse treatment services with mental, primary and general health services • Recommended the use of oral methadone • Highlighted the social and financial cost of incarcerating substance users when appropriate treatment services are available
29th meeting, 1994	• Requested that comprehensive guidelines be drawn up by the WHO, detailing the procedures and policies for treating and rehabilitating people with substance abuse issues • Called for a more careful analysis of how governments can reduce demand for drugs
30th meeting, 1996	• Focused on treatment effectiveness • Aimed to gain a greater understanding of the effectiveness of compulsory treatment in comparison to voluntary treatment • Highlighted the need to target resources to fight the spread of Hepatitis B and C through sexual activity and the sharing of needles • Considered classifying benzodiazepines in terms of their misuse potential • Decided to critically review dihydroetorphine, ephedrine, remifentanil and sumatriptan • Noted the marketing of different nicotine preparations such as gum and patches to people who are involved in cessation programs
31st meeting, 1998	• Concerned with the critical review of a number of substances following the thirtieth report of 1998, including dihydroetorphine and remifentanil • Undertook a preliminary review of gamma hydroxybutyric acid (GHB), dimethoxyphenethylammine (2C-B), zolpidem and methylenedioxyphenyl 2 butanamine (MBDB) • Although there was no significant reported abuse of MBDB and zolpidem, the other substances were sent for critical review
32nd meeting, 2000	• Reviewed dimethoxyphenethylammine (2C-B), methylthioampetamine (4MTA), gamma hydroxybutyric acid (GHB), methylenedioxyphenyl 2 butanamine (MBDB), diazepam and zolpidem • Sent amfepramone, amineptine, buprenorphine, carisoprodol, dronabinol, pentazocine, poppy straw and tramadol for preliminary review
33rd meeting, 2002	• Critical review of amfepramone, amineptine, buprenorphine, delta 9 tetrahydrocannabinol (THC) and tramadol • Dronabinol was perceived as having therapeutic uses for people suffering from weight loss due to the effect of the HIV virus and was therefore moved to schedule IV of the1971 Convention
34th meeting, 2006	• Reviewed ketamine, zalepion, zoplicone, butorphanol, oripavine and khat • Requested an educational campaign on the appropriate use of SRIs (serotonin re-uptake inhibitors)

For detailed information, see http://www.who.int/substance_abuse/right_committee/en/index.html

Table 1. Considerations by the World Health Organization Expert Committee on Drug Dependence. ILLUSTRATION BY GGS INFORMATION SERVICES. GALE, CENGAGE LEARNING

began in the mid-1950s. Discussions of the problems created by amphetamines, amphetamine-like drugs, and hallucinogens followed in the 1960s. The difficulties associated with controlling these new heterogeneous groups of drugs under the Single Convention of 1961 became apparent. At its seventeenth meeting in 1969, the committee discussed a draft Protocol on Psychotropic Substances, developed

by the UN Commission on Narcotic Drugs, which formalized a classification of psychotropic drugs developed by the expert committee at its sixteenth meeting in 1968. The increasingly serious international public-health problems created by these drugs led the United Nations to hold a conference for the Adoption of a Protocol on Psychotropic Substances in Vienna in February 1971; this resulted in the Convention on Psychotropic Substances, 1971, that the United Nations finally ratified in 1976. One important feature of this convention is that it mandates a WHO assessment of a substance prior to control and states that the WHO "assessments shall be determinative as to medical and scientific matters." This mandate added great responsibility to the functional role of the expert committee.

The expert committee did not meet formally again until 1985. In the interim, however, a number of WHO ad-hoc committees met to consider various aspects of implementing the treaty. In 1980 an extensive review of the Assessment of Public Health and Social Problems Associated with the Use of Psychotropic Drugs was carried out. To assist WHO, the U.S. National Institute on Drug Abuse, in collaboration with the Committee on Problems of Drug Dependence, published a monograph on "Testing Drugs for Physical Dependence Potential and Abuse Liability," which updated a similar WHO report published a decade earlier. A particularly difficult section of the psychotropic convention concerns exempt preparations. This involves thousands of pharmaceutical products and their handling, and had still not been resolved as of 2008, despite three meetings of WHO advisory groups in 1977, 1982, and 1984.

Initially, to handle the necessary WHO functions under the conventions, ad-hoc advisory groups met rather than call formal meetings of the expert committee. The first of these was held in 1978. In 1979 specific compounds were considered under both conventions and the recommendation was made that, in the future, compounds proposed for control under the psychotropic convention be considered by class. In 1980 nine anorectic substances (drugs that cause loss of appetite) were reviewed and recommendations as to control were forwarded. Discussions concerning khat and its active principals—cathine and cathinone—began, and a widespread group of laboratories initiated research. In 1981 the mixed opioid agonist-antagonist drugs were reviewed, and in 1981 and 1982 the benzodiazepines as a class were reviewed, and recommendations for control were sent to the UN. Also during this period a more formal method for review emerged from discussions with the UN Commission on Narcotic Drugs and the WHO executive board. Detailed critical reviews of substances to be considered for control were developed, and the Programme Planning Working Group formed to review these and suggest future classes of compounds for review by the expert committee. Two additional ad hoc advisory committee meetings were held in 1983 and 1984 to consider a variety of individual compounds and exempt preparations.

As a result of structural changes within WHO and the creation of the new Programme on Substance Abuse, in the future the expert committee will change its focus from reviewing substances for control under the international conventions to a broader consideration of the issues of prevention and reduction of demand.

See also **Abuse Liability of Drugs: Testing in Humans.**

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ZERO TOLERANCE. The phrase *zero tolerance* has come to be associated with government and private employer policies that mandate predetermined consequences or punishments for specific offenses. However, the phrase first became associated with U.S. drug interdiction during the 1980s and 1990s. Most public schools now have zero tolerance policies for firearms and other weapons as well as alcohol, drugs, and tobacco. Zero tolerance policies generally are rigid and can produce results out of proportion to the improper behavior. Nevertheless, the courts have endorsed drug-testing programs that allow employers to enforce zero tolerance policies.

U.S. DRUG CONTROL POLICY

Zero tolerance was a federal drug policy initiated during the War on Drugs campaign of the Reagan and George H. W. Bush administrations (1981–1993). Under this policy, designed to prohibit the transfer of illicit drugs across U.S. borders, no possession, importation, or exportation of illicit drugs was tolerable, and possession of any amount of illicit drugs was subject to civil and criminal sanctions. Zero tolerance was an example of a criminal justice approach to drug control. Under such an approach, drug control is the responsibility of the criminal justice system, and the use of drugs is a criminal act, with legal sanction as the consequence.

Zero tolerance is a *user-focused* strategy of drug control in which law-enforcement agents target illicit drug users rather than dealers or transporters. The rationale is that users of illicit substances create the demand for drugs and constitute the root cause of the problem. If, therefore, demand for drugs can be curbed by imposing harsh penalties on users, the supply of drugs into the country will slow.

The U.S. Customs Service initiated the zero-tolerance policy in conjunction with the U.S. Attorney's office in San Diego, California, as part of an effort to stop drug trafficking across the U.S.-Mexican border. Individuals in possession of illicit drugs were arrested and charged with both a misdemeanor and a felony offense. Customs Service officials believed the policy to be successful in reducing the flow of drugs across the border and recommended that it be implemented nationwide. Subsequently the National Drug Policy Board, in conjunction with the White House Conference on a Drug-Free America, had all federal drug-enforcement agencies implement zero tolerance in 1988 at all U.S. points of entry.

The policy did not involve enacting new laws or regulations; it only entailed instituting strict interpretation and enforcement of existing laws. In practice it meant that any vehicle—including bicycles, transfer trucks, and yachts—would be confiscated and drivers and passengers arrested if any amount of illicit drugs was discovered. The U.S. Coast Guard and the U.S. Customs Service cracked down on all cases of drug possession on the water and at all borders. If, during the course of their regular patrols and inspections, Coast Guard personnel boarded a vessel and found one marijuana cigarette or even the remnants of a marijuana cigarette, they arrested the individual and seized

the boat. Before this policy was instituted, the Coast Guard had either ignored it or issued fines when personal-use quantities of illicit substances were discovered.

Zero tolerance was criticized because federal agencies expended substantial resources to identify individual drug users instead of concentrating those resources on halting the influx of major quantities of drugs into the country for street sale. The policy of seizing boats upon the discovery of trace amounts of drugs was also controversial. Some believed the policy to be an unfair and unusually harsh punishment; seizing a commercial boat that was the sole source of income for an individual or family was denounced as being too severe a penalty for possession of one marijuana cigarette. There were some highly publicized cases of commercial fishing boats being seized on scant evidence that the boat owner was responsible for the illicit drugs found.

GENERAL POLICY

The term *zero tolerance* has a broader application than the Reagan-Bush drug interdiction approach. Zero tolerance is a perspective that maintains that any amount of illicit drugs is harmful to the individual and society and that the drug policy should prohibit any and all illicit drug use. According to the contrasting viewpoint, the simple use of drugs is distinguishable from problem drug use and, although absence of all drug use is desirable, government resources would be used more efficiently if they targeted problem users or addressed problems related to or caused by illicit drug use.

Drug testing in the workplace typically uses a zero tolerance approach. In the late 1970s employees challenged these policies in the courts. However, the U.S. Supreme Court, in *New York City Transit Authority v. Beazer*, 440 U.S. 568, 99 S.Ct. 1355, 59 L.Ed.2d 587 (1979), ruled that a city agency blanket exclusion of persons who regularly use narcotic drugs does not violate the Equal Protection Clause of the Fourteenth Amendment. This zero-tolerance decision subsequently was extended to various employment situations. By 2000 many employers routinely required a drug test as part of the employee hiring process. Applicants who fail the test usually are not hired because employers use a zero-tolerance drug policy.

Zero-tolerance policies have become a standard part of U.S. public schools. With the increase in serious and fatal school violence since the 1990s, zero tolerance weapons policies have dominated the media coverage, yet zero tolerance drug polices are also part of school rules. Zero tolerance has widespread public support, as it mandates high standards and signifies a tough stance toward drugs and school violence.

Nevertheless, there are many critics of zero-tolerance polices. Critics liken zero tolerance to mandatory minimum sentencing in the criminal justice system. Under both systems there are no exceptions made for individual circumstances; this policy results in punishments that appear excessive, such as a student suspension for bringing aspirin to school without permission.

RANDOM STUDENT DRUG TESTING

Decades of research on substance abuse and dependence have shown that prevention through education and other means is the most effective method of decreasing/eliminating the use of illicit drugs and the misuse of prescription medications. In September 2007 President George W. Bush reiterated his belief that substance abuse among the American youth can be halted through a comprehensive community approach. He stated that programs such as random student drug testing work "to help our Nation's young people make healthy choices throughout their lives and to encourage community- and family-based approaches to the challenges and risks facing today's youth."

Under the auspices of the Office of National Drug Control Policy's *Stopping Drug Use Before It Starts* initiatives, random student drug testing is considered a powerful motivator for students to abstain from drug use. Research has shown that adolescents are at their most vulnerable both to peer pressure and to the long-term damaging effects of drugs. If they can be encouraged to avoid experimenting with drugs, the health benefits are thought to be lifelong. Currently, the most highly abused drug among students is marijuana, closely followed by prescription painkillers (such as OxyContin).

To help schools combat this problem, federal funding is available for random drug testing. Currently, more than 80 school districts across the nation have received grants from the United States

Department of Education to develop, implement, or expand random drug-testing programs in more than 400 schools. Of the roughly one-quarter school districts with random drug testing programs, nearly one-third also had voluntary drug-testing programs available to all students. Nearly three-quarters of the school districts that conduct drug testing also offer substance-abuse treatment programs, either within the school physical or mental health system or by referral to allied community providers.

The U.S. Department of Education has a threefold goal: to prevent substance use and abuse entirely; to identify students who are at an early stage in their substance abuse and to provide them with resources to stop further use; and to identify students who are either at risk for or who are already substance-dependent and to refer them for appropriate treatment services and programs. In contrast to the traditional zero tolerance programs, the philosophy of the random student drug-testing programs, as administered through the U.S. Department of Education grant funding system, is nonpunitive—its focus is on prevention, early intervention, and appropriate treatment and support.

See also **Drug Interdiction; Operation Intercept; U.S. Government: The Organization of U.S. Drug Policy.**

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The *Encyclopedia of Drugs, Alcohol, & Addictive Behavior, 3rd edition* updates and expands upon the award-winning second edition of this set, addressing social, medical, legal, and political issues related to substance use and addictive behavior. New essays report on advances in the study of genetics and imaging techniques involving the brain, and on contemporary socio-political topics such as the role of drugs and alcohol in the media, the prevalence of drugs in the international sports and fashion industries, the relationship between drug trafficking and terrorism, and the impact of the Internet on drug and alcohol use. Sections on behavioral and pharmacological approaches to treatment have been extensively revised and updated. The third edition also expands international coverage of historical and modern perspectives on drug, alcohol, and tobacco use in more than 30 countries and regions, including the Caribbean, the Middle East, and China. Many of the 545 topical entries are enhanced by statistical charts, graphs, tables, and photographs.

Published by Macmillan Reference USA, this new edition was developed under the guidance of Editors Pamela Korsmeyer and Henry R. Kranzler. Pamela Korsmeyer has written about addiction, drug control and federal policy, as well as on international development. Dr. Kranzler is a professor of psychiatry and program director of the General Clinical Research Center at the University of Connecticut School of Medicine. He has authored or co-authored more than 300 journal articles, book chapters, and other publications.

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